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1858-1929

The American Journal of Obstetrics and Gynecology

VOL. XVII ST. LOUIS, APRIL, 1929 No. 4

IN MEMORIAM

GEORGE CLARK MOSHER, A.M., M.D., F.A.C.S.

AUGUST 8, 1858—JANUARY 18, 1929

DR. GEORGE CLARK MOSHER, a former president of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, was one of those rare individuals combining charming personality, marked enthusiasm, long experience and versatility of activities.

Descended from a German baron in Alsace-Lorraine, his ancestors came to America early in the seventeenth century. He was reared in northwestern Ohio, educated at Ohio State University and the Louisville School of Medicine and was really a product of the old preceptor days of medical training. In 1883 he married Ida Beagle of Blissfield, Michigan, and in 1884 located in Kansas City where he was active in practice until his death, having personally delivered over 9000 babies during his professional life.

As a leader he was responsible for improved hospital conditions especially in maternity services through the Southwest. He owned and experimented with the first "clean milk" dairy west of St. Louis, composed of the prize herd of Holstein cattle from the St. Louis World's Fair. He continually agitated maternal and child welfare work throughout the country.

He was a teacher of long experience and for years occupied the chair of professor of Obstetrics and Gynecology in the Kansas City Medical College and the medical department of Kansas University.

Widely traveled at home and abroad, a lover of art, a connoisseur of music, a master of literature and a member of numerous societies and clubs, he was president of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons in 1926.

Dr. Mosher has left a lasting influence of service and leadership indelibly written in the history of the great Missouri Valley and the vast Southwest.

G. F. P.

Original Communications

THE HEPATIC LESION IN ECLAMPSIA*

By William J. Dieckmann, B.S., M.D., St. Louis, Mo.

(From the Department of Obstetrics, Washington University School of Medicine and the St. Louis Maternity Hospital)

IN DISCUSSING the etiology of eclampsia, a disease which is characterized by so many pathologic changes in various organs and in the blood and in which a large amount of research, clinical, chemical and experimental, has already been done, it is difficult to know where to begin additional work on this subject and on which manifestation of the disease to place the greatest importance.

As the title of this paper indicates, I wish to deal with one aspect of the disease, namely, the hepatic lesion which is present in many cases of eclampsia but has never been demonstrated definitely in any other condition nor in any pregnant animal. Anyone who is interested in investigative work as regards the etiology of eclampsia can readily obtain all important information which exists concerning this disease in the admirable monograph of Hinselmann which deals with every phase of the subject and therefore a monograph which promptly gives the investigator a full review of what has already been done in this field. It is in this book that the pathologic changes which occur in the kidney and liver are so well described by Fahr. In summing up the chief characteristics of the hepatic lesion in eclampsia in the human subject, Fahr states that localized changes are found in the periphery of the lobules, and fibrin thrombi in the portal capillaries. This condition in the capillaries leads to the production of large blood spaces and hemorrhages which bring about the necrosis of the liver tissue involved, chiefly by pressure. Also in Hinselmann's monograph various authors review important facts regarding eclampsia. Bergell, who discusses the subject from a chemical standpoint, reviews various existing theories and is forced to conclude that these views can only be definitely established as facts by much additional experimental work and further clinical observation.

Recently Hofbauer, Louros, and Schmechel have given their attention to the production of pathologic lesions in the liver simulating the lesion of eclampsia. Louros and Schmechel in reviewing the literature

*Read at the Forty-first Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Toronto, Ont., September 10, 1928.

Note: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

up to 1926 mention that Ascoli, Weichard, Liepmann, Blumreich, Hoeslin and Loekmann and Theis have attempted to produce the lesion of eclampsia. But in reviewing this work they feel that there are certain objections to all these experiments that cannot be put aside, and no one has succeeded as yet in producing a condition similar to eclampsia clinically, nor has anyone produced a typical lesion in the liver. Louros and Schmechel's work was carried out by injecting acetylcholin, clavipurin and histamin. They were impressed with the fact that clinically there exists a constriction of peripheral circulation while the circulation internally, particularly that involving the splanchnic area was definitely widened. They called attention to the fact that in eclampsia due to the unstable vasomotor mechanism there is a marked drop in blood pressure in the eclamptic following delivery, the patient frequently going into shock. It is this clinical

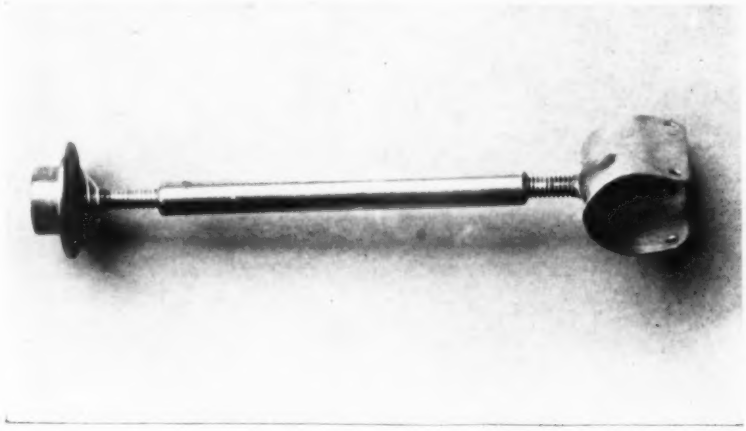

Fig. 1.—Blankenhorn cannula. Placed around portal vein through which injections to portal vein are made.

condition, first referred to by Schwarz, which led them to use the above-mentioned drugs in their experimental work, hoping to simulate both from clinical and pathologic standpoint the conditions which exist in eclampsia. As we are only interested in their results in the liver, we shall merely include their remarks on their findings in that organ. They found a marked widening of the liver veins in general, with hemorrhages from the veins and capillaries associated with marked cell changes, differences in staining properties in nuclei as well as definite necrosis of the liver cells. There was also a marked necrosis of the liver. Bile stasis, a finding which Fahr referred to in the human lesion, was recognized. Unfortunately, they show no illustrations of their lesion, and therefore one is not able to judge definitely the extent of the pathologic picture. About the same time Hofbauer attempted to produce the liver lesion as well as other manifestations

of the disease by using histamin in small doses over a long period of time. In summing up his work Hofbauer states that there was produced peripheral necrosis of the liver both anemic and hemorrhagic in type associated with the formation of thrombi and bile stasis. He shows several illustrations of these lesions, and if they illustrate the most striking of his findings, one is forced to believe that the lesions produced were not particularly marked or extensive.

The theory I express in this paper regarding the possible means of producing the hepatic lesion experimentally is based on rather different reasoning. In the first place in human pregnancy one is impressed with the fact that the syncytial tissue and chorionic villi as a whole are considerably different from those in the placenta of various

Fig. 2.—Liver of dog. Normal portal space showing branch of portal vein, bile duct, and hepatic artery.

experimental animals, and in the human subject these elements enter the blood quite readily, particularly so in the latter weeks of pregnancy. These elements being protein in nature must be broken up by certain neutralizing substances which most likely are the proteolytic enzymes of the blood. Another fact which has impressed me is that the lesion of eclampsia is a specific one and is primarily produced as a result of thrombosis of the small tributaries of the portal vein in the periphery of the liver lobule; therefore, substances which are concerned in the production of this lesion must be present in greater concentration in the portal system than in the general circulation. These toxic substances, as far as the liver is concerned, must have properties of injuring the endothelial cells or, on ac-

count of the nature of the substance, shorten the coagulation time, or have both properties. Considering this, the most logical assumption is that substances must be absorbed from the intestinal tract. It may be well to mention here the fact that clinically, if a patient undergoes a strict dietary régime in the later weeks of pregnancy with a limitation of proteins from the diet, meat proteins in particular, substituting a diet high in carbohydrates and with a good intestinal elimination emphasized at the same time, such patients rarely if ever develop eclampsia.

Several years ago I became interested in the serologic work of Obata. Obata reported that if normal serum is incubated with saline extract of fresh placenta the latter is no longer toxic to mice if in-

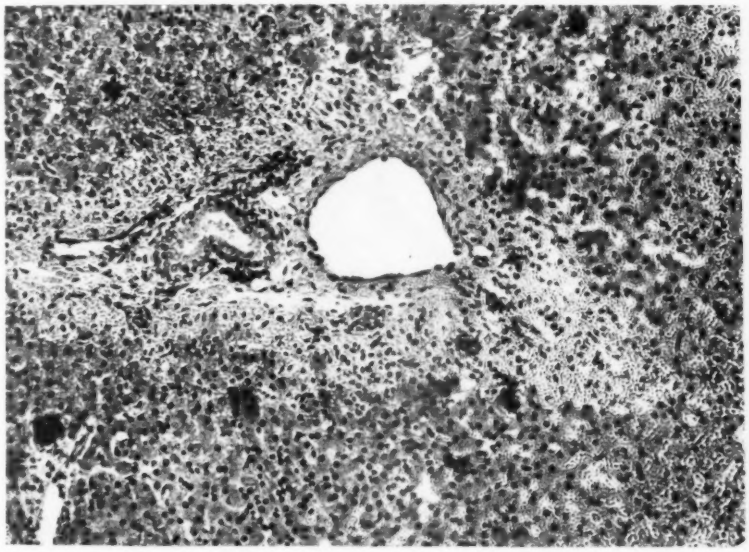

Fig. 3.—Dog No. 10. Liver, showing hemorrhage into connective tissue of portal space as well as adjacent liver tissue with necrosis of liver cells. Comparative early lesion. Lesion most strikingly seen in right lower portion.

jected intravenously. On the other hand the serum of an eclamptic patient obtained during a convulsion or shortly after does not possess this power. After the convulsions have ceased or very early in the puerperium the serum has regained full neutralizing power. I repeated the work of Obata and reported it on two occasions, and I was able to confirm his work in every detail so far as I carried it out. This work suggested to me that the neutralizing substances of the blood in eclampsia were used up or bound and that similar substances of protein derivation which now entered the portal system from the intestine were not broken up or neutralized and, therefore, had the opportunity of shortening the coagulation time in the portal system and resulting in thrombosis in the tributaries of the portal vein. This

idea was further developed by the various publications of Mills on so-called tissue fibrinogen and its effects on the clotting time. Two of these papers are particularly applicable in discussion of the present subject. Mills presented a paper entitled "The Absorption and Excretion Through the Kidney of Complex Protein Substance Tissue Fibrinogen," an abstract of which follows.

The surprising discovery was made that the complex protein phospholipin compound, tissue fibrinogen, may readily be absorbed from subcutaneous, intraperitoneal, or oral administration, and may make its way equally well to all parts of the body. It may even be excreted unchanged in the urine of animals. Given in any of these ways, its specific quickening effect on blood clotting is in evidence in all parts of

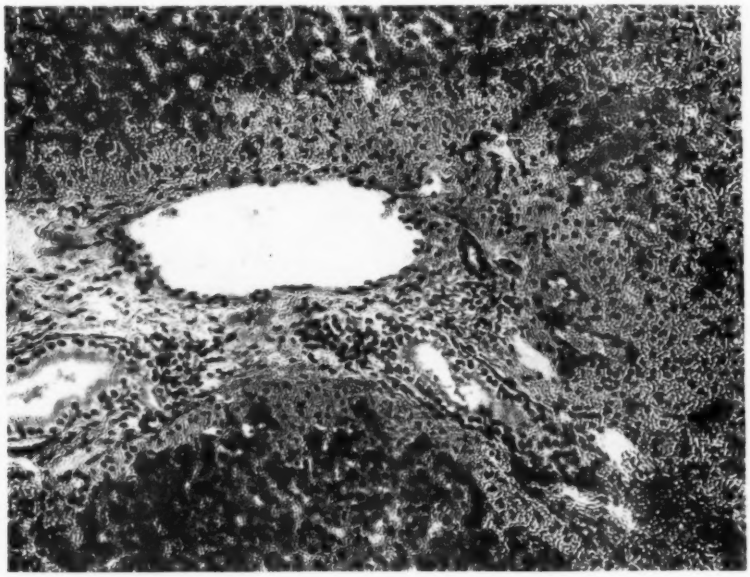

Fig. 4.—Dog No. 10. Similar portal space showing more extensive lesion; hemorrhage and necrosis at the periphery of liver lobule; most marked in right half of picture.

the body, so that hemorrhage at any point is better controlled than by local application of the coagulant to the bleeding area.

Given subcutaneously, the effect of the coagulant comes on in about an hour and lasts eight to ten hours. One c.c. of a 1.5 per cent solution of the substance produces a 40 per cent to 50 per cent shortening in the clotting time of the blood. Apparently no ill effects accompany the use of even enormous doses. However, even very small amounts injected intravenously are very dangerous and are liable to produce intravascular clotting and death.

The results of intraperitoneal injection are similar to those just described above, except that the absorption is more rapid and the effects are over in six to eight hours.

Most important of all, however, is the discovery that the tissue fibrinogen is very rapidly absorbed from the small intestine without previous digestion, being taken directly into the blood and exerting its specific effect on blood clotting within

two to five minutes. When so administered to animals in large doses, it is found to be secreted by the kidneys in its original active form. It must, therefore, pass through the tissues of the body with the ease of a crystalloid substance in spite of its extreme complexity. The ease with which such a colloidal natural body compound permeates throughout the organism at once raises the question as to why the cell colloids do not themselves also diffuse out. The findings here would indicate that they are entirely capable of so diffusing if they are once free but that they are probably held in proper place in the cell by chemical union. In other words the integrity of the cell is not maintained by the nondiffusibility of the constituents present but by their chemical combinations.

The method of accomplishing the successful oral administration of the coagulant to man depends on its rapid passage through the empty stomach and into the intestine before the juices have a chance to act upon it, and on a dilution of these juices by following the coagulant with at least one-half pint of water. Ice water is

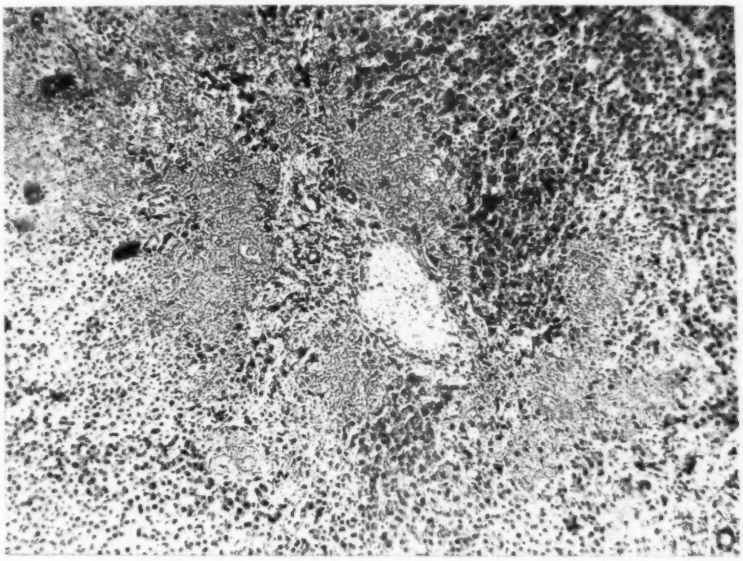

Fig. 5.—Human liver, showing portal space typical of lesion of eclampsia, hemorrhage and necrosis and marked deposition of fibrin around portal space extending from the periphery to the lobule.

preferable as it stimulates active peristalsis, passing the fluid quickly through the stomach and distributing it over a maximum of absorbing area in the small intestine. Larger doses are required when taken orally, and the effect is more brief in duration. The speed of the absorption and the quick effect provide an emergency measure in bleeding cases. If necessary, a more prolonged action can be obtained later by the hypodermic injection. It is obvious that an empty stomach is a necessary prerequisite to successful oral administration. Either the HCl or pepsin of the gastric juice would very quickly destroy the effectiveness of the coagulant.

It is most striking to observe a drop of 50 per cent to 70 per cent in the clotting time within three to five minutes after proper oral ingestion of the substance.

The physiologic questions involved in this rapid intestinal absorption of undigested protein are many. Certainly it opens up a new field for consideration along this line.

The other paper of Mills of particular importance is "Effect of Food Ingestion on Clotting of the Blood"; an abstract of this also follows:

The clotting time of the blood is the longest before breakfast in the morning but shows only slight variations at this time on successive days. It shortens 30 per cent to 40 per cent about an hour after each meal and two to three hours later begins to lengthen. Five or six hours after each meal it will be almost at the same point as on rising in the morning. This clotting time observed before each meal is termed the basal clotting time.

The cause of this effect of food ingestion remains in obscurity. The clotting time bears no relation to the specific gravity of the blood so far as physiologic variations go. Water taken produces no change in the clotting rate; neither does glucose solution nor the eating of plain sugar candy. Coagulated egg white pro-

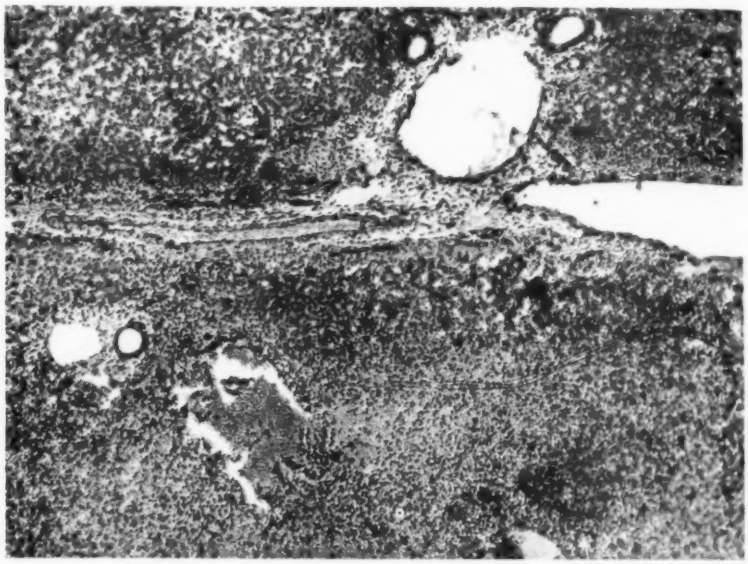

Fig. 6.—Dog No. 10. Liver, showing fairly large portal space with portal vein and bile ducts, marked hemorrhage and necrosis throughout lower half of picture.

duces no change until about the end of an hour when the typical increase in coagulability of the blood occurs.

The effect on the blood then seems to depend on the presence of the food in the intestine. Whether it is absorbed material that produces the change cannot be said. Acid or alkali ingestion sufficient to markedly alter the reaction of the urine produces no change in the clotting time.

Another fact which is worthy of mention in the discussion of tissue fibrinogen is the fact that the fibrinogen content of the blood is increased in pregnancy, and sometimes very high figures are obtained in cases of eclampsia.

Considering these facts I felt that the lesion of eclampsia could be produced by substances entering the portal circulation from the intestine. Under normal conditions these substances were neutralized or broken up there, but on account of the fact that the neutralizing

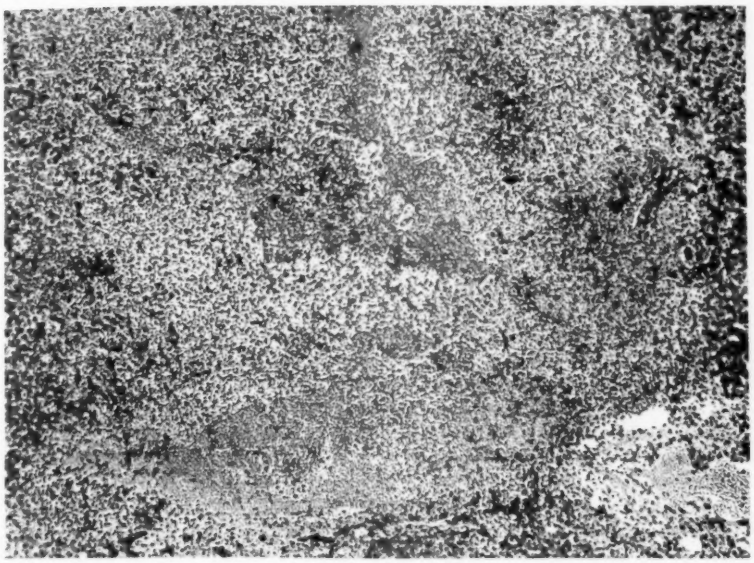

Fig. 7.—Dog No. 10. Liver, showing marked area of hemorrhage and necrosis extending from the periphery of the lobule and involving a large area of liver tissue.

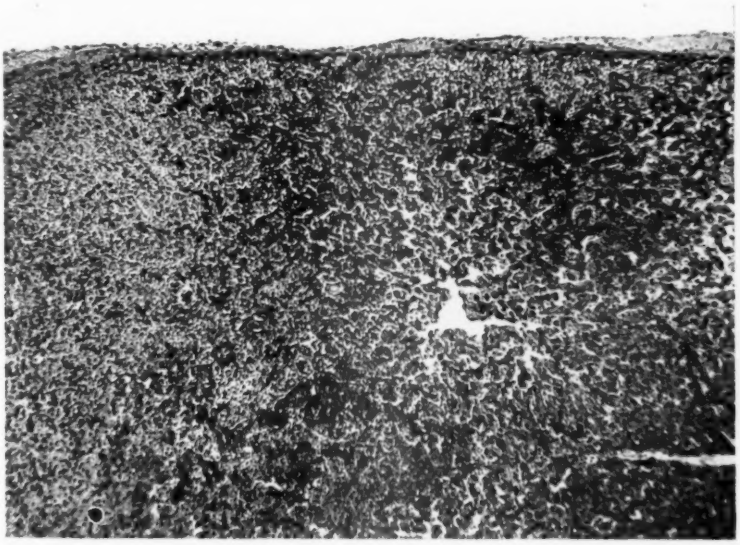

Fig. 8.—Dog No. 10. Liver. Periphery of liver, showing capsule with hemorrhage in capsule tissue and in periphery of lobule with marked necrosis. Large necrotic area in upper left portion of picture, another one immediately below capsule just to right of center.

substances, proteolytic enzymes, if you will, were being used up in the general circulation due to action against constantly entering placental elements, these absorbed substances of protein nature, consisting of tissue fibrinogen or the like, could cause a marked decrease in the coagulation time in the portal system with resulting thrombosis in the portal capillaries.

In carrying out my experiments pregnant animals were not used because the relation of the placenta to the general circulation is entirely different from those in the human subject. As tissue fibrinogen from the work of Mills seemed to have all the properties necessary to simulate the condition which was occurring in human pregnancy as

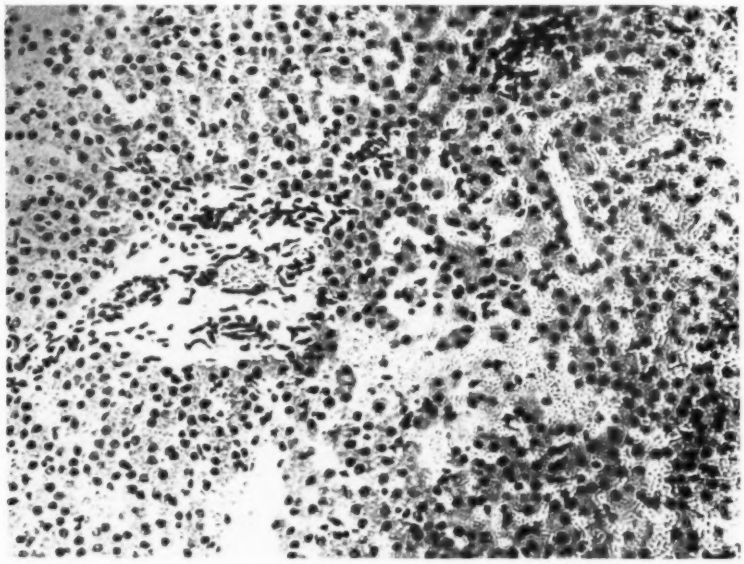

Fig. 9.—Dog No. 16. Liver, showing small portal space with small artery, vein and bile duct. Early lesion. Hemorrhage into tissue of portal space and entering adjacent liver tissue in all directions, more marked on right side where hemorrhage is fairly extensive with considerable destruction of liver cells.

result of protein material entering the circulation, this substance was considered suitable for use. In preparing extracts of tissue fibrinogen myself, I found that the content in the placenta was quite equal to that in the lungs, which indicated that tissue fibrinogen could enter the circulation from the placenta as a source.

I had expected to begin my experiments by injecting tissue fibrinogen in the peripheral circulation and giving it at the same time by mouth. A cannula devised by Blankenhorn to obtain specimens from the portal vein came to my attention, and before trying the oral experiment I thought it was advisable to use the Blankenhorn cannula and to inject directly into the portal vein to see actually what the substance would do under these conditions. Therefore the Blankenhorn

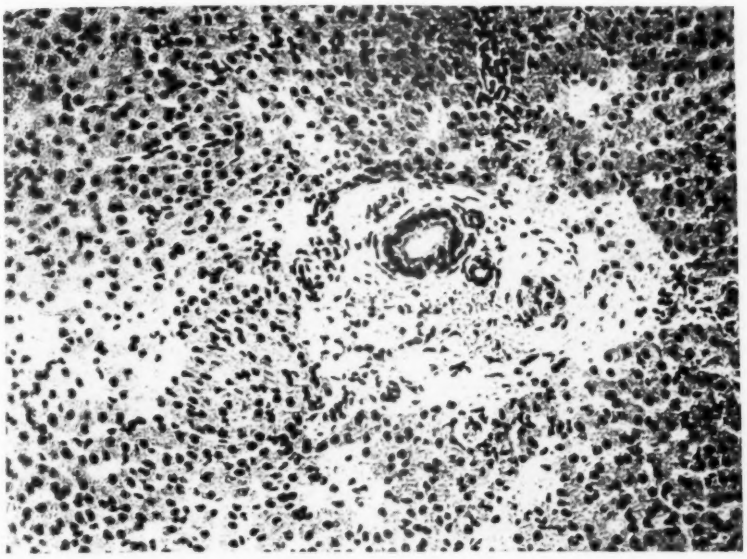

Fig. 10.—Dog No. 16. Liver, showing another small portal space, artery, vein and bile duct with hemorrhage into the interstitial tissue of portal space and extending from it in all directions. Lighter area represents areas of hemorrhage between liver cells. Note irregular contour due to this hemorrhage. Definite necrosis of liver cells.

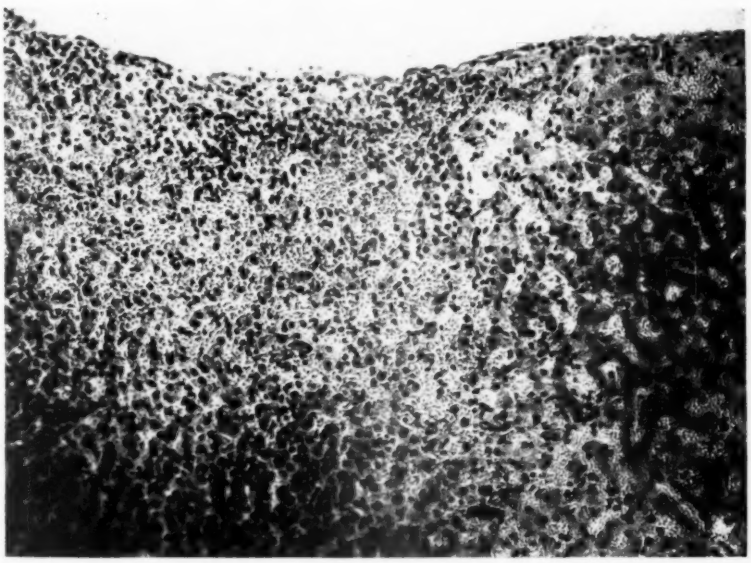

Fig. 11.—Dog No. 14. Liver, showing extensive hemorrhage and necrosis in periphery of lobule under capsule. This lesion was very marked; no lesion around portal space was found in this case because of general thrombosis of portal vein due to overdosage.

UNIV. OF MICH.

Fig. 12.—Dog No. 14. Portal space, showing branch of portal vein, bile duct and hepatic artery. Marked thrombosis of portal vein. When a thrombosis of this extent occurred further hemorrhage in periphery of lobule was not possible. This was a frequent finding due to overdosage in portal vein. In none of these cases, however, was the portal vein outside the liver involved.

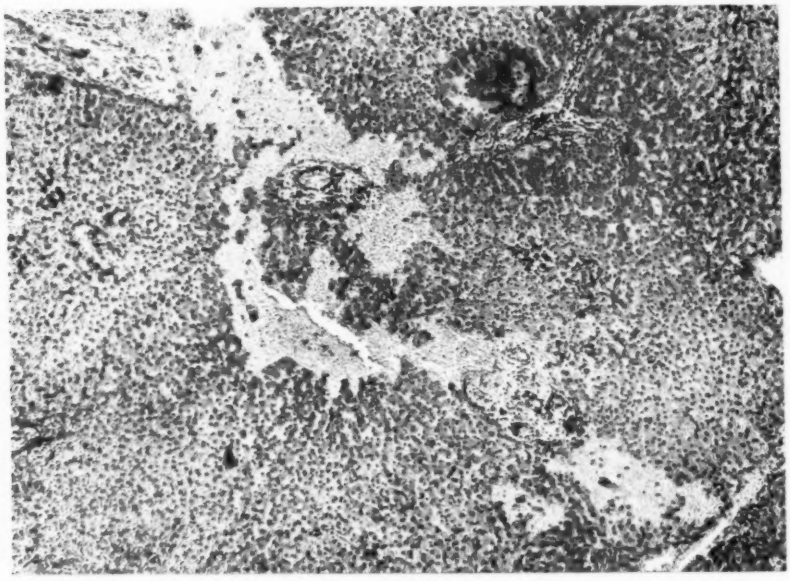

Fig. 13.—A small portal space is seen just above the center and slightly to the left practically completely surrounded by a large hemorrhage. Just below the center and to the right is another portal space in which and from which there is a marked extravasation of blood.

cannula was used for injections of tissue fibrinogen in the portal system at the same time the animal was receiving doses of tissue fibrinogen in the peripheral circulation. The tissue fibrinogen used was that of Merrell made according to Mills' formula.

The dogs were usually anesthetized with ether although amytal was used on a few. Sandbags were placed under the lower thoracic vertebrae to make the portal vein more accessible. A midline incision was made extending up to the xyphoid. The portal vein was easily located and exposed distal to its junction with the splenic vein. Two heavy silk sutures were passed under the vein, and the saddle part of the cannula was tied in place. The skin was separated by blunt dissection for a distance of 2 cm. to 3 cm. away from the line of incision, to a point corresponding to the natural location of the button. The fascia muscle and peritoneum were perforated with a Kelly clamp, and the button was slipped through. It was

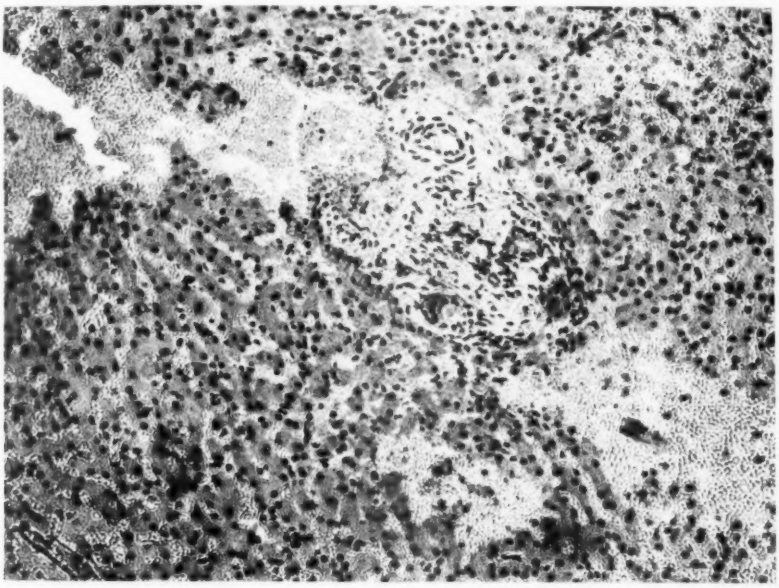

Fig. 14.—A higher power of Fig. 13. Shows lower portal space in Fig. 13 with marked extravasation of blood from it and within the interstitial tissue.

then connected to the saddle, the sandbags were removed and the length adjusted. An injection into one of the small mesenteric veins was made at the time of operation. The closure was in layers, silk being used. For injection the dog was strapped down, tissue fibrinogen injected into the femoral vein and then into the portal vein. Aspiration in the latter was always made before and after injection. The dogs were killed with ether whenever sick or at the end of three to five days. They were autopsied immediately, and the tissue was placed in 10 per cent formalin. The doses of tissue fibrinogen used varied from 2 c.c. to 5 c.c. for peripheral circulation, 6 c.c. to 12 c.c. for portal circulation.

Eight dogs were handled successfully in this way. In three of these dogs extensive lesions were found which in every way simulated the lesion of eclampsia. Dog No. 10 showed this lesion particularly marked, and it is from this case that our illustrations are chiefly taken. The liver showed marked hemorrhage in the periphery of the lobule with extensive necrosis. There were many areas in which

the lesion was found quite characteristically in early stages. The portal vein showed fresh thrombosis, but these were only found in the smaller branches in this case. Dogs, Nos. 14 and 16, from which illustrations are also taken, show early lesions which are quite characteristic. Here the thrombosis of the portal vein was more extensive. I feel this resulted from overdosing and prevented further extension of the lesion by preventing hemorrhage. The remaining five dogs all showed marked thrombosis of the portal vein with some evidence of peripheral necrosis and hemorrhage. These lesions were chiefly found in the periphery of the liver and directly under the capsule. It is interesting to mention in this connection that Fahr quotes Orth and Kauffmann as stating that a thrombosis in the portal vein does not give rise to the eclamptic lesion; this occurs only when the small capillaries of the portal vein are involved in the thrombosis. Overdosing obviously caused this condition in our animals. The description of the lesions produced is given in the legends accompanying the illustrations.

CONCLUSIONS

This work so far as it has been carried shows that tissue fibrinogen, when injected into the portal vein accompanied by injections of the same substance in the peripheral circulation, produces marked portal thrombosis. If the dosage is kept within the limits for the individual dog, a marked peripheral necrosis with hemorrhage can be obtained as three animals clearly demonstrated. I feel that this work so far as it has been carried is very encouraging, and I hope to be able to show that the same condition can be produced by oral administration. I believe these experiments show that there is some real background for my theory, and if by further work I can produce the lesion through peripheral injection and oral administration, this would be sufficient evidence to explain the lesion of eclampsia in the liver and answer the question why the preventive treatment of eclampsia, namely, limiting of protein diet in the last months of pregnancy and good intestinal elimination, has been so effective.*

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*Since the presentation of this paper, I reported before the Society of Experimental Biology and Medicine (St. Louis Branch) our results with peripheral injection and oral feeding of tissue fibrinogen.

This report is based on the combination of the peripheral injection and oral feeding of tissue fibrinogen. Seven dogs were fed fibrinogen in 3 ml. doses through a stomach tube and at the same time injected 1 to 5 ml. peripherally. These experiments varied from three to seven days in duration. In seven cases, three showed liver hemorrhage in the gross, similar to that in eclampsia, four showed beautiful eclamptic lesions, and 6 showed portal vein thrombosis within the liver. One was entirely negative. Case 28 is a good example of the combination of peripheral and of oral administration of tissue fibrinogen. The liver in this case showed marked hemorrhages throughout, which extended inward from the periphery of the lobule. This lesion was found in various stages of development throughout the liver, but in most instances it was very marked (See Figs. 13 and 14).

IS SURGICAL INTERVENTION JUSTIFIABLE IN THE TREATMENT OF METROPHLEBITIS AND THROMBOPHLEBITIS OF THE PELVIC VEINS?*

By John Osborn Polak, M.D., Brooklyn, N. Y.

(From the Long Island College Medical School and Hospital)

THE answer to this question will depend upon our ability to properly interpret certain clinical and pathologic data which have been observed during the course of these infections, at operation or at autopsy. Furthermore before we decide to elect radical surgical treatment, there are four basic propositions which must be weighed and considered, i.e.:

1. Can thrombophlebitis be recognized by its symptoms and physical signs with sufficient accuracy and at such a time as to warrant subjecting the woman to the added risks of a serious operation?

2. Do the pathologic processes and biologic defenses which are revealed at operation, at autopsy and in the laboratory justify intervention?

3. Are the indications for the operation so clean cut that needless surgery is not done?

4. And finally has the mortality been actually reduced by operation?

Of course it is understood in this discussion that we are not considering that form of thrombophlebitis, known as phlegmasia alba dolens, the treatment of which is established and not debatable. However, such is not the case in septic metrothrombophlebitis (puerperal pyemia) which carries with it, according to the statistics of Sippel, Bumm, Seitz, Seegert, Opitz and others, a mortality which ranges from 50 to 100 per cent. It is apparent therefore that any procedure which offers the slightest hope of increasing the proportion of cures is worthy of discussion and of trial.

If we accept the surgical principle that an infected organ should be removed before the infection spreads beyond its confines, involves the surrounding structures, and reaches the peritoneum or blood stream, it seems reasonable for us to remove or block this focus of infection as soon as the diagnosis is established. However, the difficulty in making a positive diagnosis constitutes one of the chief objections to radical operation.

Infection of the uterine veins is always secondary to intrauterine infection and the bacteria concerned are identical with those found in the endometrial lesion. Hence, there is always a history of a pre-

*Read at the Forty-first Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Toronto, Ontario, September 10-12, 1928.

existing puerperal endometritis which is followed, when metrophlebitis develops, by the clinical syndrome of repeated chills, fever, and sweats with temperature remissions. The blood culture is usually negative and the white blood cell count, the platelet count, and the polymorphonuclear percentage are commonly low. Bimanual examination of the pelvic organs gives little or no aid, except to exclude the presence of peritoneal and parametrial exudates.

J. W. Williams in his classic paper on this subject claims that the thrombosed veins may be palpated as tender worm-like masses in the broad ligament by rectoabdominal touch. An extensive clinical experience with several hundred of these cases convinces me that the diagnosis must be based upon the history and clinical picture, not on the physical signs, as the tactile sense is seldom able to differentiate the thrombosed veins from coincident parametrial lesions, for there is always some degree of cellular inflammation (periphlebitis) associated with thrombophlebitis. Therefore the diagnosis must depend on the clinical sequence and unless one is familiar with the physiologic and pathologic changes which are taking place in involution and which are retarded by the presence of an endometrial infection, one can hardly appreciate the significance of the symptoms which make up the clinical picture, their sequence or the strength of nature's biologic defenses.

Following the separation and expulsion of the placenta, the placental site contracts and retracts, its area is diminished and the large venous sinuses which have furnished the blood supply for the uteroplacental circulation become plugged with thrombi. As retraction continues and involution progresses, the veins in the uterine wall are obliterated by thrombus formation or new vessels of smaller caliber are formed within the old ones, the original vessel being plugged or lined with thrombus. This aseptic plugging and obliteration may be changed into an infective process by a coincident puerperal endometritis which retards contraction and retraction. The thrombi become inoculated with pathogenic bacteria, identical with those found in the endometrial lesion. These multiply within the clot, erode the intima, liquefy the thrombus and escape into the circulation in droplets of pus or in infected emboli causing pyemia. Their multiplication may be so rapid or the cellular defense of the individual so poor that they reach the blood stream in pure culture without exciting any degree of cellular reaction in the tissues through which they pass. On the other hand if the cellular reaction of the blood is sufficient or the infecting organisms are of low virulence, additional defensive clotting and rapid cell proliferation in the wall of the vein will take place.

Metrothrombophlebitis must therefore be regarded as a defensive reaction against the spread of infection and the periphlebitis dis-

tinctly protective just as is the leucocytic wall and the layer of small round cell proliferation in the basal endometrium and contiguous myometrium which confines an endometrial infection to the uterine cavity. When contraction and retraction are maintained only hemolytic strains of bacteria have the power of penetration.

It is evident from this description that in a relaxed uterus or in the presence of active bacteria, thrombus formation may extend out beyond the uterine wall through the ovarian, uterine, hypogastric, iliac, and femoral veins in nature's attempt to block the bacterial advance by a succession of thrombotic bulwarks. Erosion of the intima not only stimulates thrombus formation but excites a prompt protective tissue reaction in and about the wall of the vein. This observation is supported by the studies of Bardelofer who has demonstrated that the vessel wall provides resistance to the egress of the streptococcus. With the entrance into the vein of certain strains of bacteria, notably streptococci and Bacillus coli, there is erosion of the lining endothelium which, as already stated, causes coagulation, clot formation and excites cell proliferation in the wall of the vein and in the surrounding tissues, with a resulting phlebitis and periphlebitis.

Within the clot the bacteria rapidly multiply, liquefy the clot and escape into the contiguous channels only to be blocked again by new clot formations. The multiple small purulent foci found in the inflamed thrombosed veins of the uterine wall and in the venous radicals of the pampiniform plexus are usually surrounded by a more or less well defined cellular tissue reaction, which in many instances is sufficient to limit the infection to the veins of the myometrium and of the true pelvis. Manipulation and operation merely break down this protection and spread the infection to the blood stream. Could we determine clinically just the time when this process is confined to the veins of the uterine walls or when the bacterial advance is temporarily blocked by thrombus formation, distal ligation, extirpation and drainage might save some lives, but on the other hand many women would be needlessly operated upon as nature's defenses are sufficient to effect a cure in many instances. When the infective thrombosis extends to the common iliac, renal and vena cava with the formation of multiple infective emboli, which may be carried to the liver, spleen, lungs, pleura, heart, joints, and brain, it is apparent that any operation is fruitless. It must be conceded therefore that the success of operation, whether hysterectomy or ligation, depends on early diagnosis and must be done before these patients become poor operative risks.

Postmortem studies of the deaths credited to puerperal sepsis show that metrothrombophlebitis is present in over 50 per cent and in

these cases multiple embolic foci in the lungs are almost constant findings. *Early diagnosis made on the sequence and clinical syndrome is therefore all important.*

In nearly all cases of thrombophlebitis some form of intrauterine manipulation has preceded the onset, as for example intrauterine manipulation in the treatment of placenta previa or manual removal of the placenta or curettage of the relaxed uterus for the removal of retained fetal remnants or there is a history that the uterus owing to excessive blood loss, the presence of submucous myomas or coincidental constitutional disease favors bacterial invasion of the clots in the placental site.

Firm contraction and retraction offers the strongest barrier against the extension of endometrial infection and endometrial infection is the most common puerperal lesion. The first symptoms are those of endometritis, evidenced by arrested involution, profuse

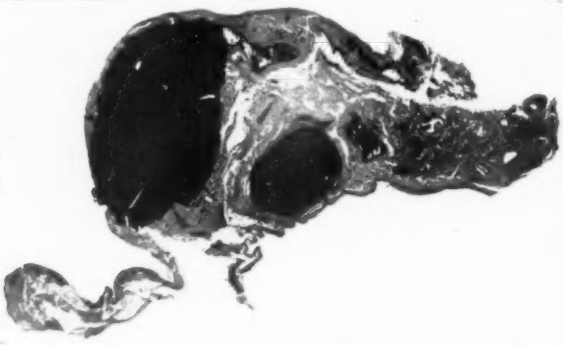

Fig. 1.—Section through the left broad ligament. Veins are thrombosed. The supporting stroma is infiltrated with moderate numbers of leucocytes. Necrobiosis of the tissues has commenced.

red lochia, uterine colic (afterpains), with the passage of clots and a moderate pyrexia. These symptoms of endometrial inflammation are soon followed by the clinical syndrome of chills, fever, and sweats with temperature remissions. Repeated rigors indicate bacterial escape beyond the confines of the clot. A rise in temperature to 104° to 106° F. immediately follows the chill. This is evidence of the excessive defensive cellular activity and in turn is succeeded by a sudden remission in temperature to normal or subnormal with a profuse sweat which shows that the venous extension is temporarily blocked by new clot formation. This in a few hours is again liquefied, and the clinical syndrome is repeated. The pulse rises with the temperature but has not the proportionate fall, for the toxemia rapidly weakens the heart muscle and its effect is shown in the pulse. The cellular elements of the blood undergo a rapid destruction, shown in the falling hemoglobin percentage, the rapid diminution of the red cell count, the leucopenia,

and the low platelet count, all of which indicate lowered individual resistance. Anemia and wasting rapidly develop and the woman's prostration becomes extreme, though in the early stage of the disease the patient may feel fairly well and be able to take food in the interval between chills.

In the foregoing discussion we have noted that the diagnosis must be made on the clinical syndrome and also that nature is effecting a barrier to bacterial advance by the cellular reaction in and about the vein. The question is, what are the indications for surgery?

A thorough review of the literature gives us little definite information. The statistics are made up of gross and corrected mortalities, the advocates of early operation using the latter to support their con-

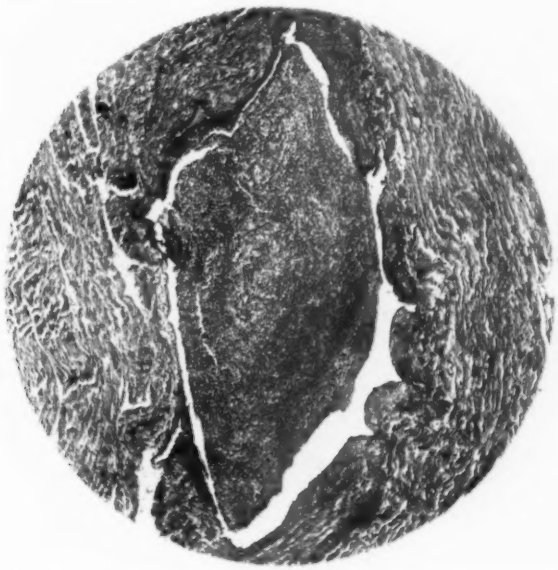

Fig. 2.—Septic thrombus in veins at the placental site. Thrombus has partially retracted from the walls; is comprised almost entirely of polymorphonuclear leucocytes.

tention, while their opponents point to the high gross mortalities in order to justify their conservatism. No one has laid down clean-cut indications which can be followed by the rank and file. We all know that many of these cases recover without surgery.

J. F. Baldwin writes me in answer to my query as to how we may recognize the case that will be benefited by operation. "That diagnostic acumen cannot be transmitted, that his success has been dependent upon his ability to recognize the case which will not recover without surgery. He does a panhysterectomy and has a noteworthy series of successes which in all probability would have been death in less skillful hands. He does not clear the situation for us. Huggins who has long had the courage of his convictions, states "that the case where operation is of value is one which lies between the milder form of the disease where the

temperature and pulse variations are not so wide and where, from the beginning the patient does not show evidence of very serious involvement, and the acute fulminating variety where the progress is rapid and grave, from the beginning. Between these two groups we find a class of cases which is prone to become chronic and where, in about eight or ten days after the onset of the infection one is gravely perplexed as to what will happen from day to day." "It is at this particular time, early in the history of the case, and before the patient has become repeatedly saturated with the infection, and where a certain amount of poison is being thrown into the circulation daily which results in lowering her resistance, that operative treatment should be instituted." Cases which have been ill for more than four weeks in Huggins' opinion, offer little hope from surgery.

While I may be classed among the ultraconservatives, I have felt for many years that there must be some time in the course of the

Fig. 3.—Capillary sinuses of uterine wall, 8 mm. from the endometrial surface. The vein is filled by a partially retracted thrombus comprised largely of polymorphonuclear leucocytes; blood cells and fibrin are occasionally noted.

disease when an operation could be successfully performed. In our clinic we have been unable to determine the indications or the exact period at which we should interfere and we are frank to say that we cannot see from the study of reported cases that Baldwin, Huggins or other advocates of surgery present us with any clean-cut indications for operation. It is just the class of cases which these men select for hysterectomy, ligation and drainage which in our clinic recover with small repeated blood transfusions, quinine injections and vaccine therapy. Why these women do get well we do not know, but the fact remains, that more than 60 per cent recover, if all pelvic manipulation is avoided. This point cannot be too strongly stressed. On the

other hand our mortality from operation has been 100 per cent. Of course this may show our ignorance in the selection of cases. The fact that a single vein is involved in the majority of cases, appears to be the chief point of encouragement for the advocates of surgery.

In a study from the literature of 197 cases at the time of operation, but 1 spermatic vein was involved 75 times, 2 spermatics 5 times, 1 hypogastric 6 times, 1 hypogastric and 1 spermatic 6 times, and 1 common iliac was involved 8 times; this shows that in 100 cases in this series, but one vein was involved in 89, while, in the remaining 97 the thrombosis was diffuse. It would therefore appear from this study, that in a little more than 50 per cent of this selected group successful operation was

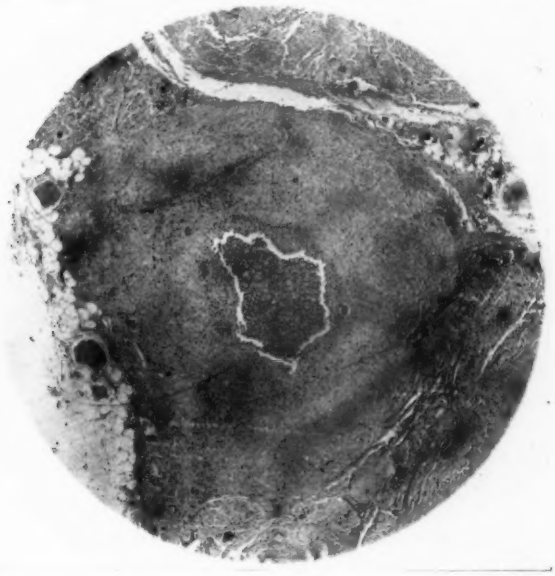

Fig. 4.—Thrombosed vein in the broad ligament. The lumen is filled by a thrombus comprised largely of polymorphonuclear leucocytes. Exudate has also extended into the intimal coat.

possible. However, manipulation necessary to find the limits of the thrombosis is not without danger, for nature has almost always established a more or less complete protective cellular reaction to extension of the infection. This was shown in 31 cases autopsied by Seegert: in 26 he found pure thrombophlebitis with complete obliteration of the vessel lumen, and in 5 thrombophlebitis with marked periphlebitis involving the associated lymphatics, which illustrates that in even those cases which end fatally the local focus is surrounded by cellular defense.

Operation at the time of complete occlusion is unnecessary, for nature has accomplished what we expected to do by ligation without

the manipulation and shock. Mortality figures in the cases in which surgical intervention has been employed are always unreliable, for no man can tell the case which will recover without surgery. Operation to be successful must be done when the patient is a fair risk and surgery may, and, in our opinion, often does turn the tide against us.

In 182 cases selected from the literature which were subjected to transperitoneal ligation (Table I) there were 94 deaths, or a gross mortality of 51.6 per cent. In the corrected list we find 111 cases which are considered as favorable surgical risks with 34 deaths, or 33.9 per cent mortality. Huggins' corrected mortality figures which are not included in this table, are 33.3 per cent. Contrast these results with those reported by B. C. Hirst: 37 cases conservatively treated,

TABLE I. SUMMARY OF TRANSPERITONEAL OPERATIONS

	TOTAL	DEATHS	GROSS MORTALITY	FAVORABLE CASES	DEATHS	CORRECTED MORTALITY
1 spermatic vein excised	35	17	51.1	20	4	20.0
1 spermatic vein ligated	35	15	44.1	26	7	26.8
Ligation or excision of both	20	8	40.0	16	4	25.0
Ligation or excision of 1 sperm. and 1 hypogastric vein	15	6	55.5	10	1	10.0
Ligation and excision of both spermatic and 1 hypogastric	9	5	29.0	6	2	33.3
Ligation and excision of both spermatic and hypogastric	17	5	92.3	12	1	8.3
Ligation and excision of 1 hypogastric	14	12	71.4	10	8	80.0
Ligation and excision of 1 spermatic and common iliac	14	11	83.3	11	7	66.6
Ligation of Vena Cava	6	5	76.9			
No details	17	10	16.9			
Average	182	94	51.6	111	34	33.9

with 5 deaths, or a mortality of 13.5 per cent and the 63 cases from our own clinic with 19 deaths, and I feel that our conclusions are justified.

Our experience, which is drawn from observations and autopsy and laboratory studies, together with years of conservative support leads us to the following conclusions: (1) that thrombophlebitis is a conservative process which follows upon an endometrial infection not confined to the uterine cavity, owing to the poor contraction and retraction of the uterus, (2) that there is always cellular reaction in and about the vein, (3) that the clinical syndrome is clean-cut but the physical signs are lacking or misleading, owing to the fact that there is always some periphlebitis present, (4) that any manipulation, bi-

manual examination or operation breaks down nature's protective barrier, (5) that the indications or the time to institute surgery are not definitely established, (6) that the septic woman is admitted by all to be a bad surgical risk, and (7) finally, that the mortality from operation, even in the best clinics does not warrant subjecting the woman to surgery.

20 LIVINGSTON STREET.

COMPLETE LACERATIONS OF THE PERINEUM AND THEIR SURGICAL TREATMENT*

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AN EXAMINATION of my personal records dating from June, 1917, to June, 1928, shows that during this period of eleven years, I had operated upon 42 patients for complete or third degree lacerations of the perineum. Five of these patients were operated upon shortly after labor. Another, a child seven years old, had a complete repair of the perineum for a traumatic laceration involving the perineal body, the sphincter ani muscle and the anterior rectal wall. She was operated upon shortly after admission to the hospital. The others had secondary repairs.

PROPHYLAXIS

Much has been written, during the last decade, on the prevention of complete lacerations of the perineum. As a matter of fact, this complication of childbirth may be avoided, in most instances, by giving proper attention to the perineum during delivery. There are two types of prophylactic measures recommended in order to avoid this accident, first, incisions of the perineum, and second, manual dilatation of the perineum and vagina.

Two types of incisions are in use: the median, which is referred to as a perineotomy and the lateral which is known as an episiotomy. The advocates of the episiotomy object to the perineotomy on the grounds that if the incision is extended by the advancing head it may go through the sphincter ani muscle. This, however, is not a sound reason and may be avoided by operatively extending the incision in such a way that it encircles the anus on one side, thus saving the sphincter. As a general principle, it is probably better to employ a lateral incision when considerable room is required, and a median when the opposite obtains. The lateral episiotomy is done on the side toward

*Read before the Forty-first Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Toronto, Ont., September 10-12, 1928.

which the occiput points, in other words, a right episiotomy in a right position and a left episiotomy in a left position. Very rarely is it necessary to make an incision on the two sides.

Incisions of the perineum are generally performed on primiparae, although they are sometimes necessary on multiparae. A multipara who has had an episiotomy or an extensive repair of the perineum with her first labor, comes to a second with external genitals resembling those of a primipara, and in addition having a scar where the union of the severed tissues took place; it may, therefore, become necessary to again incise the perineum at this delivery. The same applies to the multipara who has had a secondary repair of the perineum for a serious laceration.

PERINEAL INCISIONS VS. DILATATION OF THE PERINEUM

Those who favor manual dilatation of the perineum and vagina before delivery state that this procedure obviates the performance of perineal incisions. While this method will overcome a resistant perineum, it not infrequently results in the separation of the levator ani muscles under the intact mucous membrane and skin. As a result of this a rectocele will soon appear. This condition practically never occurs after well sutured perineal incisions.

The absence of any large rectocele in the 42 cases operated upon for complete laceration of the perineum tends to show that it is not the tearing of the perineum which is responsible for this lesion, but rather the stretching and the relaxation of the fascial structures of the posterior vaginal segment.

IMMEDIATE VS. LATE REPAIR

It has been my custom to repair this type of laceration immediately after the expulsion of the placenta when I see the patient after delivery. Five such cases were treated and all of them obtained excellent results. Their puerperia were not prolonged nor complicated as a result of this repair. On the other hand, if the parturient is not seen soon after delivery, at least three months are allowed to elapse before operating. At this time involution has taken place, the edema has disappeared, scar tissue has formed between the torn edges and better operative results are obtained than when the operation is attempted a few days after labor.

TECHNIC OF OPERATION

The pelvic floor is opened by an H-shaped incision. The lateral incision, on each side, extends from a point below the duct of the vulvovaginal gland to the retracted end of the sphincter. The transverse incision joins the two lateral by running through the edge of the scar

Fig. 1.—Complete laceration of the perineum involving the sphincter ani muscle and the anterior rectal wall.

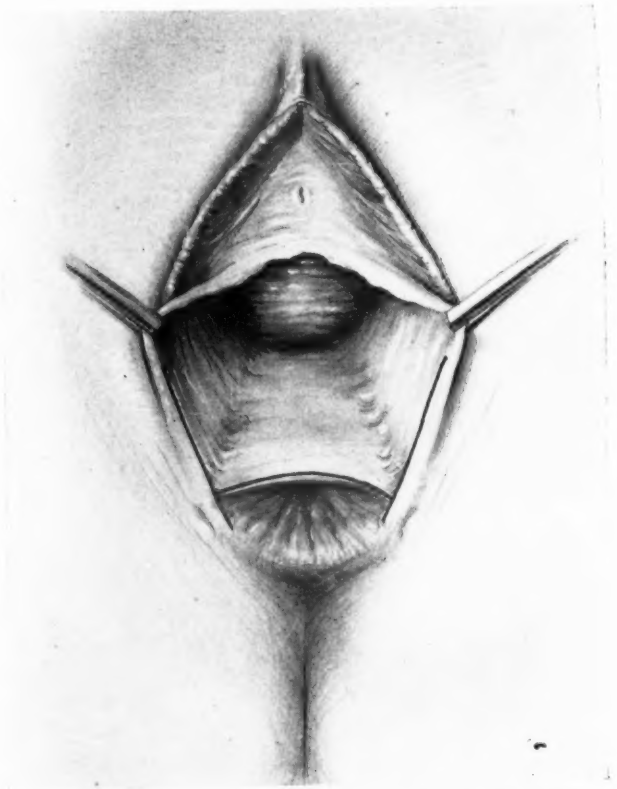

Fig. 2.—Opening the pelvic floor. The incision is H-shaped. The lateral incision, on each side, extends from a point below the duct of the vulvovaginal gland to the retracted end of the sphincter. The transverse incision joins the two lateral by running through the scar tissue uniting the rectal and vaginal walls.

Fig. 3.—The vaginal flap has been raised. The rectum is separated from the levator ani muscles, by blunt dissection.

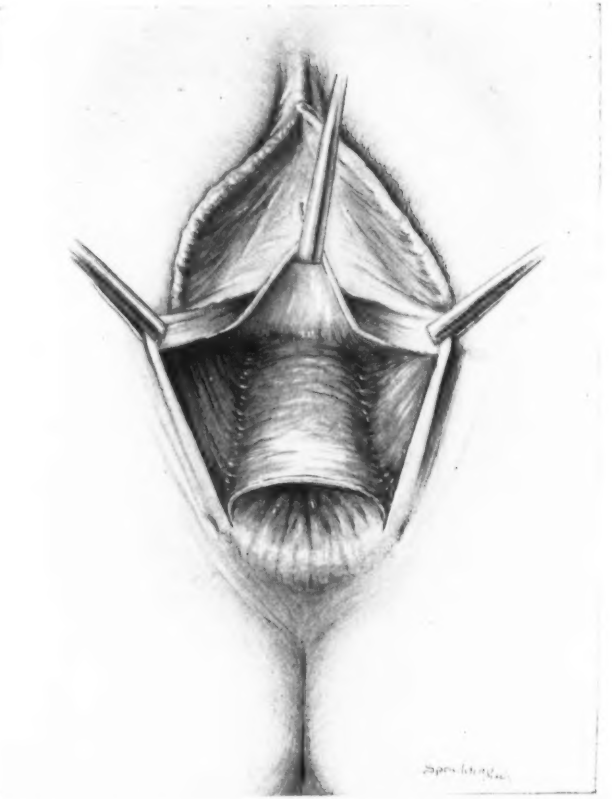

Fig. 4.—The denudation is completed and the individual structures are exposed.

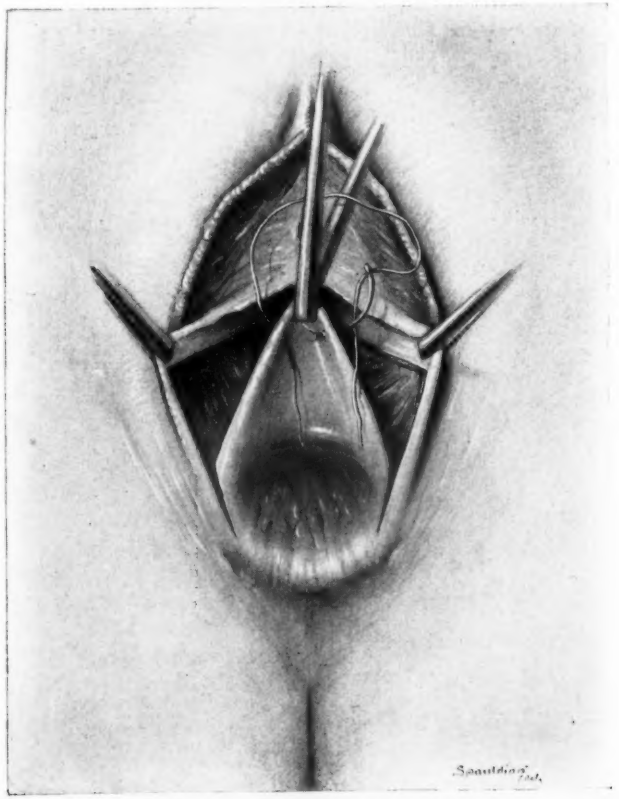

Fig. 5.—The anterior rectal wall is picked up by an Allis forceps and put on stretch. The anterior rectal wall is united by interrupted sutures of linen thread, the knots being tied within the bowel lumen.

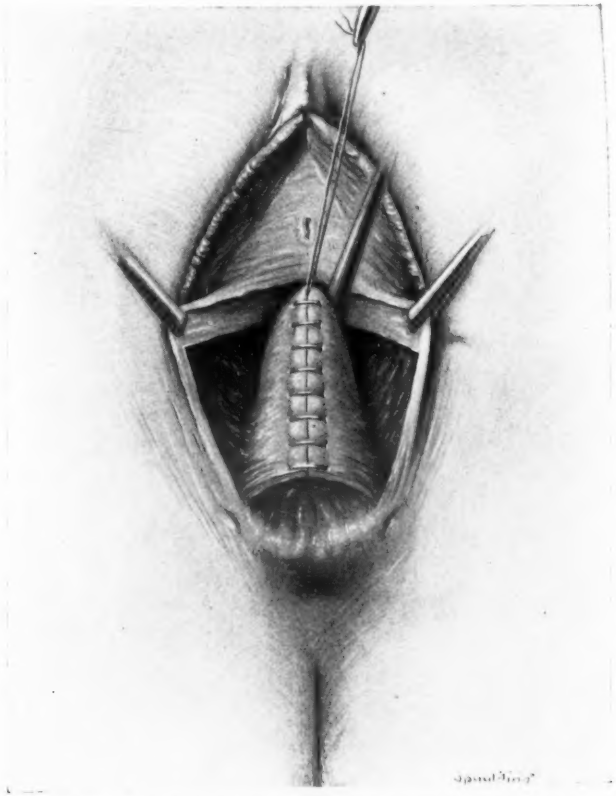

Fig. 6.—The first layer of rectal sutures is completed.

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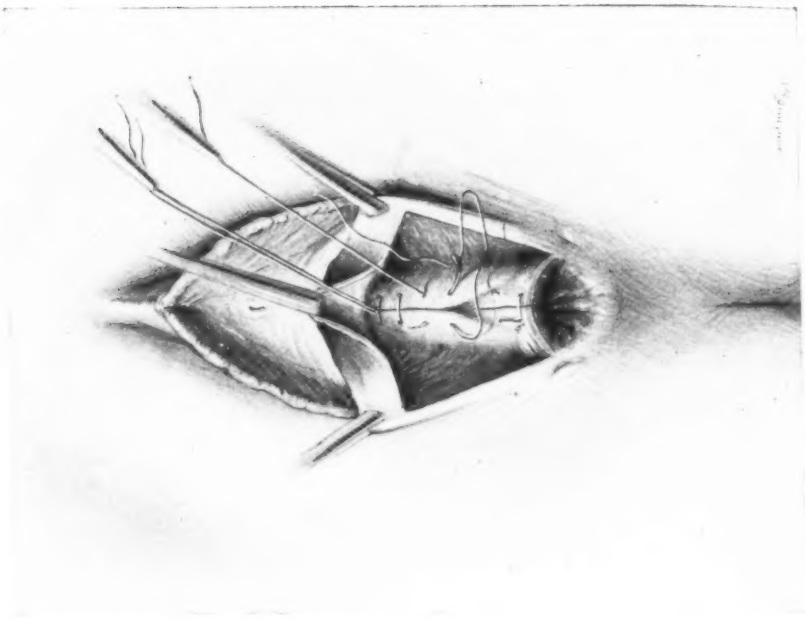

Fig. 8.—The perirectal tissues are further approximated by figure of eight sutures of No. 0 chromic catgut. The rectal wound is thus closed in three layers.

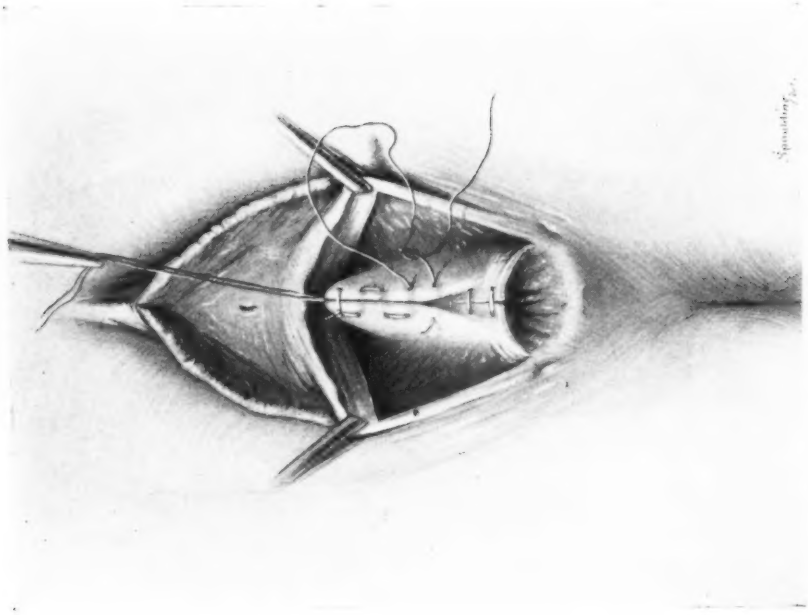

Fig. 7.—The perirectal tissues are approximated over the first suture line by a continuous mattress suture of No. 0 chromic catgut.

chromic catgut.

wound is thus closed in three layers.

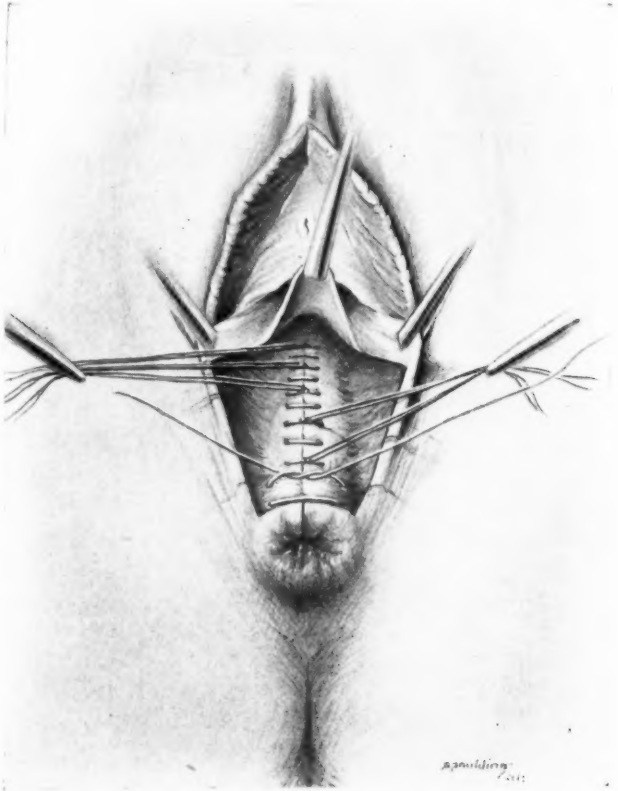

Fig. 9.—The rectal suture is completed. A figure of eight suture of No. 1 chromic catgut approximates the torn ends of the sphincter ani muscle.

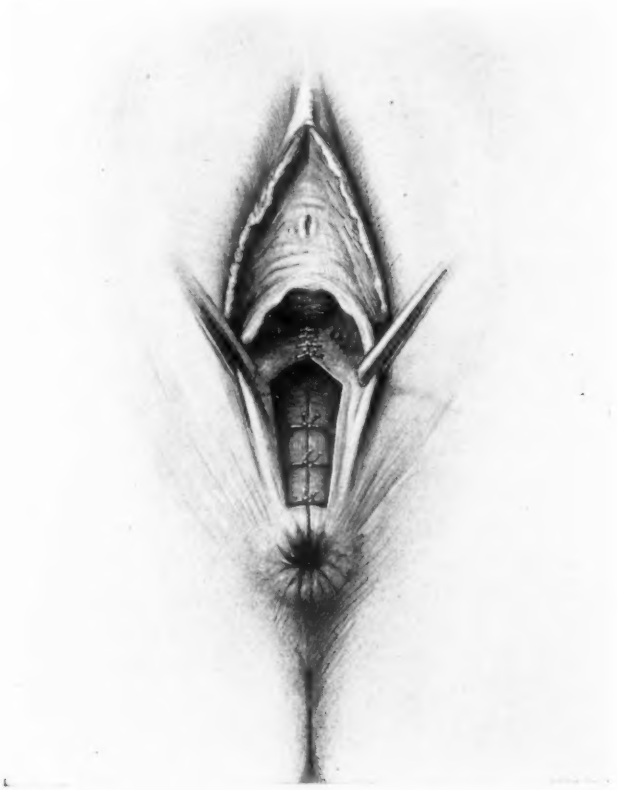

Fig. 10.—The excess of the vaginal flap has been resected. The vaginal wall has been approximated with interrupted sutures of No. 2 chromic catgut. The levator ani muscles covered by their fascia are united by three interrupted sutures of No. 2 chromic catgut.

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tissue uniting the rectal and vaginal walls. A flap of posterior vaginal wall is raised exposing the rectum which is separated from the levator ani muscles by blunt dissection. The anterior rectal wall is picked up by an Allis forceps and put on stretch; the torn edges are united by interrupted sutures of linen thread, the knots being tied within the bowel lumen. The perirectal tissues are approximated over the first suture line by a continuous mattress suture of No. 0 chromic catgut. The perirectal tissues are further approximated by figure of eight

Fig. 11.—The external perineum has been closed with interrupted sutures of No. 2 chromic catgut. These sutures, in their course, pick up the united levator ani muscles to obliterate dead space. A subcuticular stitch may be substituted for the interrupted sutures. The final result of the operation is shown.

sutures of the same material. The rectal wound is thus closed in three layers. The torn ends of the sphincter ani muscle are dissected out of their bed of scar tissue and approximated with a figure of eight suture of No. 1 chromic catgut. The excess of the vaginal flap is resected, the edges of the vaginal incision are united with interrupted sutures of No. 2 chromic catgut, and the levator ani muscles, covered by their fascia, are brought together by three interrupted sutures of the same catgut. The external perineum is closed by interrupted sutures of

No. 2 chromic catgut which in their course pick up the united levator ani muscles to obliterate dead space. A subcuticular stitch may be substituted for the interrupted sutures.

AFTER CARE

We have followed a definite routine, which has proved satisfactory, on the Gynecological Service of the Carney Hospital. For the first five days the diet consists of the white of an egg, an ounce of strained orange juice and enough water to fill a glass. This is given every three hours during the day and at the same intervals at night if the patient is awake. Between these hours she is given as much water as she cares to take. On the sixth day a cup of beef tea or strained broth is substituted for the albumen mixture. The morning of the seventh day the patient is given an ounce of castor oil by mouth, six hours later six ounces of warm sweet oil is gently instilled in the rectum, she is given a low soap suds enema when the desire to empty the bowel becomes apparent, and she is instructed not to strain. After this a soft diet is allowed and by the ninth day she is on a full diet.

A vaginal douche consisting of one quart of Dakin's solution is given, through a soft rubber catheter, morning and night after forty-eight hours.

Catheterization of the bladder is resorted to every twelve hours if the patient does not void readily.

SUMMARY OF CASES

	Cases
Fresh complete laceration of the perineum	6
Old complete laceration of the perineum	18
Complete laceration of the perineum with involvement of anterior rectal wall	13
Complete laceration of the perineum with involvement of anterior and posterior rectal walls	1
Complete laceration of the perineum and rectovaginal fistula	4
Total	42

OPERATIONS PERFORMED IN ADDITION TO THE REPAIR OF A COMPLETE LACERATION OF THE PERINEUM

	Cases
Dilatation and curettage	6
Trachelorrhaphy	7
Amputation of cervix	6
Anterior colporrhaphy	8
Interposition operation	4
Vaginal panhysterectomy	1
Incision of fistula-in-ano	1

In three cases of complete repair of the perineum, a small rectovaginal fistula developed because of infection. These three fistulas were closed at a second operation.

The lacerations were the result of childbirth in forty cases. In the case of one child, seven years old, it was traumatic, and the laceration was due to falling on a picket fence. In another child, also seven years old, it was due to rape.

END-RESULTS

The final result was satisfactory in all these patients, three of whom had to be operated upon twice because of small rectovaginal fistulas which had developed from improper healing due to a low grade infection in the wound. All obtained excellent sphincter control and satisfactory perineal bodies. Five of the women were subsequently delivered of living children by the low cervical cesarean section.

270 COMMONWEALTH AVENUE.

UTEROTUBAL INSUFFLATION FOLLOWED BY PREGNANCY IN 205 CASES OUT OF A SERIES OF 2000 CASES OF INFERTILITY*

AN ANALYSIS OF THE FACTORS INVOLVED WITH SPECIAL REFERENCE TO THE THERAPEUTIC APPLICATION OF THE METHOD

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THE method of peruterine tubal insufflation (transuterine tubal inflation) was originally devised for the specific purpose of determining tubal patency or nonpatency thus eliminating the necessity of an exploratory laparotomy. The diagnostic method has met with gratifying approval from all parts of the world.

At this time I feel it a sacred and pleasant duty to express to the many interested investigators my deep gratitude for their aid in the steady development of this method. Without these efforts the method could not have attained its present usefulness.

Although my interest was primarily in the diagnostic possibilities of this nonoperative procedure, it was early realized that the method might also prove to be therapeutic.

Peterson and Cron,[1] and Rongy,[2] were among the first to stress the therapeutic aspect. Special notes and reports on the therapeutic effect of tubal insufflation were made by Aldridge,[3] P. N. Charbonnet,[4] E. Douay,[5] Francillon,[6] H. Fuchs,[7] G. Frommolt,[8] F. Geppert,[9] E. Graff,[10] A. Hamant,[11] Hirst and Mazer,[12] G. Kaboth,[13] M. Lobe and J. Dalsace,[14] S. R. Meaker,[15] C. F. Morkane,[16] E. Pribram,[17] P. Romeo,[18] M. Samuel,[19] Marie von Scheller,[20] G. Schwarzwaller,[21] H. Sellheim,[22] P. Titus,[23] and others. I was able to report upon 101 cases of pregnancy in a paper read before the obstetric section of the Royal Academy of Medicine in London, October, 1925.[24] In that report no detailed attempt was made to analyze the factors involved in tubal insufflation which accounted for the successful results obtained. Since

*Read at the Forty-first Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Toronto, Ont., Sept. 10-12, 1928.

1925 I have observed a little more than an equal number of cases of pregnancy following insufflation. It may now be timely in the light of this additional experience to evaluate the rôle of peruterine tubal insufflation in the treatment of sterility.

Dickinson and Cary,[25] writing on *Sterility, Analysis of Cures and Failures* state: "The distention of closed tubes by gas, air or fluid presents as yet no comparative series of sufficient numbers to gauge results." It is hoped that the present analysis of the factors involved in 205 cases of pregnancy following the use of uterotubal insufflation will be a beginning in this direction and that other reports will soon follow to add, to modify or to corroborate the findings presented at this time.

Here it may at once be acknowledged that sterility comprises a number of other factors besides obstructed tubes, and that due and adequate attention must be given to pathologic conditions in the male as well as the female which interfere with the reproductive function, whether the disturbance be primary in the genital organs or secondary to some remote organic or general constitutional abnormality. It is perhaps necessary to mention this point because through overzealous enthusiasm for one special procedure, other important elements in the consideration of a sterile marriage are sometimes apt to be disregarded or not sufficiently stressed.

The term sterility may now be somewhat reinterpreted in the light of what has been accomplished in diagnosis and therapy. Reynolds has emphasized the term infertility. This implies the possibility of a temporary lowering of fertility which is amenable to treatment and removes the stigma of absolute hopelessness in the prospect of bearing offspring. What was regarded and still is perhaps by many as an absolute cause of sterility, as for example tubal occlusion or tubal ablation, may sometimes be remedied by surgical intervention. Giles[26] writing in 1919 on *Sterility* considers "tubal disease one of the quite definite and incurable causes of secondary sterility as it is of primary sterility."

In recent years salpingostomoplasty, tubal reimplantation into the uterus as practiced and reported by Cullen,[27] Cotte et Bertrand,[28] Riess,[29] Shaw,[30] and Unterberger,[31] and ovarian transplantation into the uterus as first done by Estes,[32] Franck,[33] Mayer,[34] Morris,[35] Palmer Dudley,[36] Tuffier et LeTulle,[37] have occasionally resulted in eventual conception taking place. Though success has not frequently followed these comparatively newer procedures, accumulating reports of successful cases cannot fail to encourage workers in this field of medicine, not to speak of the anxious childless women who are heartened by any favorable case that may come to their attention. In the same way may be regarded that large group of cases of childlessness where one conception or more has resulted either in an early miscarriage or in still-

birth, or even a normal full-term only child that may have died shortly after birth or some time before puberty. These women having once enjoyed the experience of parenthood are all the more eager for a child to satisfy the maternal instinct.

I

STATISTICAL ANALYSIS OF 205 PREGNANCIES OUT OF 2000 CASES OF INFERTILITY PRIMARY AND SECONDARY STERILITIES

The present series of 205 cases of pregnancy are taken from 2000 consecutive cases of sterility in my private practice.

The actual total number of pregnancies occurring out of 2000 cases of sterility is not known because no systematic questionnaire has ever been sent out to these patients. The data were obtained by voluntary information received from the patients or friends referred by them for treatment of sterility.

There were 1070 primary sterilities and 930 were secondary sterilities. Of the 205 who became pregnant 132 cases were primary, and 73 cases were secondary sterility. Thus although the proportion of primary to secondary sterility is as 10:9, the proportion of pregnancies occurring in both types of sterility is practically as 10:5. In my first series of 101 pregnancies there were 63 cases of primary sterility and 38 of secondary sterility, almost the same proportion obtaining as for the 205 cases. If this ratio is supported by a larger series, it will indicate that the woman who has failed ever to conceive (involuntary primary sterility) has twice the better chance of becoming pregnant as a result of treatment than the woman who has become sterile following one or more abortions whether spontaneous or induced.

There are many questions involved in this analysis. Some of them indeed may be of the greatest importance. An exhaustive analysis would require more time and labor than I have been able to devote at present. It is hoped this will be done. I feel that only a beginning has been made. For example it would be interesting to know the complete status of the genital organs of the female and of her general constitutional condition; to know the potency of the male, etc. I shall not go into the numerous causes of sterility, though this is always tempting in a discussion of therapy, but shall limit myself to the part played by tubal insufflation. In this paper only a few of the historic data bearing on etiology will be included.

THE EVENTUALITY OF PREGNANCY IN THE 205 CASES

The data with regard to pregnancy following tubal insufflation available in the 205 cases show that 188 had full-term children, and 17 had early miscarriages (8.3 per cent of the 205 cases pregnant).

Peterson and Cron[1] reported 3 abortions at the third month and 10

full-term pregnancies out of 13 women who reported themselves pregnant following transuterine inflation.

These figures are interesting because the question always arises as to the possibility of the greater predisposition on the part of these women to abort or to have pathologic offspring.

Of the 68 cases which I have personally attended following peruterine tubal insufflation there were in all 77 children born. Forty-five were boys, 3 of whom were of a second pregnancy, and 32 girls, of whom 9 were of the second pregnancy. The larger number of boys is explained by the fact that the pregnancies resulting from x-ray stimulation are included in this series and as has been pointed out in 1926,[41] the boys outnumber the girls in the ratio of practically 6 to 1, at least as far as a small series of x-ray stimulation cases is concerned.

Three women of the 68 cases aborted; 1 at four months, 1 at three months and the third 3 times (at four, five and five months). These patients suffered from delayed periods. From my own study of these particular cases associated with habitually delayed periods they appear to exhibit a greater tendency to abort than women whose menstrual function is normal.

This relatively high incidence of abortions in the group of cases not receiving personal attention, i.e., 14 out of 137, was due in all likelihood to two factors: (1) they belonged to the oligomenorrhea group of sterile patients and were not aware of being pregnant until bleeding began; (2) they did not take the extraordinary care during the early weeks and months of pregnancy which is so essential in the treatment of infertility. Attention to this point as is well known determines either early interruption or pregnancy carried to near term or to full term.

If we abstract from the pregnancies those resulting from x-ray treatment, the proportion of girls would be slightly greater than boys or about the same.

EXTRAUTERINE PREGNANCY

In 3 cases under my own observation out of the total series of 2000 cases of infertility an extrauterine pregnancy followed some time after tubal insufflation, i.e., once in 666 cases.

Conditions demanding operative procedures are apt to be followed by pelvic adhesions particularly about the tubes and ovaries which may interfere with conception. Appendicitis occurring in youth obviously has a graver import for the future in the case of girls than boys. (A larger series will be reported bearing on this point.)

THE TIME FACTOR IN STERILITY

In any consideration of treatment of sterility it is important to take account of the question as to how long after marriage shall we wait before encouraging a married couple to seek medical relief.

From three to four or five years has previously been regarded as ample time to judge a sterile marriage. This figure is obviously arbitrary, for some women have become pregnant long after this interval.

Several of the cases seeking advice for their failure to conceive were married a relatively short time. One young woman was ardently desirous of an offspring for personal reasons the chief of which concerned the question of an estate. Another had witnessed the difficulty encountered by two older sisters who became pregnant from three to five years after marriage. Another patient was well over thirty-five years of age and felt she had but a short time for childbirths left to her. She sought advice within a few months after marriage. Several had been married to a first husband for a number of years without issue or having had an only child dead or alive. They did not wait long after consummating a second marriage to find out why it did not prove fertile. Thus there are various circumstances: social, economic, domestic and some of private personal nature that impelled these patients to seek a solution out of their difficulty to conceive.

II

The present analysis was further undertaken to determine (1) whether or not tubal insufflation has a therapeutic value and (2) what are the circumstances or evidences demonstrating this fact. The evidence necessary to prove a therapeutic efficacy of the method as adduced from my case histories is based on several fundamental factors.

1. The age of the woman must be thirty years or over.
2. Pregnancy must follow within a month or at most two months after tubal insufflation.
3. The length of marriage must be three years or longer.
4. The case must not be treated by any other measure than by tubal insufflation.
5. The insufflation must be done within the first two weeks of a last regular period or in the preovulation phase.
6. Repeated insufflation accompanied by a relatively lower pressure and hence normal patency on a second, third or fourth test and followed by pregnancy may be assumed to be helpful.
7. A high initial pressure during insufflation indicating as it does some abnormality in patency is followed by pregnancy. Under such circumstances pregnancy may be assumed to be a sequel of the test.
8. Patients must not have taken precautions for at least one year prior to insufflation.

The ages of the patients becoming pregnant are of particular interest in connection with the question of the therapeutic effect of insufflation. They are divided in five groups.

There were 66 who were between twenty and twenty-five years old;

83 were between twenty-five and thirty; 49 were between thirty and thirty-five; 4 were between thirty-five and forty, and 1 was over forty years old. Two histories did not give the precise age.

In other words 54 women were thirty or over, i.e., about 27 per cent of the women who became pregnant were thirty or over, so that one should not be inclined to discourage a married couple from seeking cause for their failure in conception. They deserve every consideration, and if therapy consists only in proper instruction as to sex hygiene and general regimen, happier results may be thus achieved than by putting them off until they have been married several years.

In any analysis of end-results of a therapeutic procedure in sterility it is necessary to know what is the expectancy of conception among married couples after an undisturbed length of time.

The Publication by G. Kaboth and J. Kleefisch[43] on the conception probability in childless marriages has an important bearing on this matter. They have shown that out of 5,331 cases whose marital history they investigated, the conceptional chances of the women reckoned in successive six-month periods after marriage for spontaneous conception was found to be as follows:

After	2 years' sterility	9.9 % became pregnant.
	2½	8.14%
	3	10.5 %
	3½	6.3 %
	4	3.4 %
	4½	6.0 %
	5	6.3 %
	5½	4.9 %
	6	4.9 %
	6½	3.4 %
	7	Practically none (3 conceptions out of 922 pregnancies)

Of the 73 relative sterilities in my series 38 had failed to become pregnant for three years following the last full-term pregnancy or abortion; 17 for five years; 11 for seven years; 5 between seven and ten years and 2 for longer than ten years (1 for twelve years; and 1 for fourteen years). Of the 132 primary sterilities, 72 were married for three years; 34 from three to five years; 15 from five to seven years; 6 from seven to ten years; and 3 for longer than ten years (2 for twelve years; 1 for fourteen years). In two histories the length of marriage was not stated.

The time elapsing between the last menstrual period and the performance of tubal insufflation is also of particular interest in connection with its therapeutic application. In 15 cases this was done within the first three days after the last menstrual period; in 149 cases it was done between the fourth and fourteenth day following the cessation of the last period; in 22 cases during the third week of the menstrual cycle; in 14 cases the last menstrual period was given as

twenty-two days to one year. These 36 cases were associated with varying degrees of delayed menstruation. There were 15 cases in which no data were recorded with reference to the definite time after menstruation in which the test was performed. In normally menstruating patients the time of choice was within one week from the last menstrual period and next in preference the second week after menstruation.

The time elapsing between the performance of tubal insufflation and conception according to months was as follows:

59	pregnancies	occurred	within	1	month	after	insufflation.
39	"	"	"	2	months	"	"
15	"	"	"	3	"	"	"
18	"	"	"	4	"	"	"
8	"	"	"	5	"	"	"
13	"	"	"	6	"	"	"
152							

Thus there was a total of 152 out of 205, or 75 per cent who became pregnant during the first six months after performing the test.

Twenty-eight became pregnant during the second six month period after the insufflation; 12 became pregnant within the second year period following insufflation; 5 within the third year; 2 within the fourth year, and 1 within four and three-fourths years after the tubal insufflation.

In 5 cases the data regarding the time elapsing between the tubal insufflation and the pregnancy is not definitely recorded.

Sterile patients are more apt to report a pregnancy following a short period after peruterine insufflation than later because they themselves regard the procedure as therapeutic.

Of the greatest significance from the therapeutic side is the fact that 59 or a little more than 28.6 per cent of these women become pregnant within a month and 39 within the second month following the tubal insufflation; making 98 cases in all who became pregnant within two months, or nearly 50 per cent.

I have elsewhere[24] called attention to the importance of this short interval following tubal insufflation as a criterion of the therapeutic value of the method. If in addition such pregnancy takes place after an infertile marriage of five or more years, we possess a more definite proof of the therapeutic value of insufflation.

If we divide a series of 59 cases in which the tubes were insufflated according to weeks after the last regular menstrual period it will be seen that 24 patients became pregnant within the first month after insufflation when the latter was done the first seven days after the last menstrual period. Twenty-five became pregnant within a month after insufflation carried out the second week after the last menstrual

period. Five became pregnant within a month when the insufflation was performed during the third week following the last menstrual period. In one case pregnancy followed within a month after an insufflation done one month after the last menstrual period. In 3 of the 59 cases the exact date of the test with respect to the last menses is not stated. As the test was preferably not carried out after the second week after menstruation the six women becoming pregnant after an insufflation done later than the first two weeks of the menstrual phase were patients whose periods were habitually delayed. The test was also carried out on days later than the second week after menstruation in a few instances because the patients came from out of town and could not wait for the more preferable time.

The most significant point about these figures is that although pregnancy can follow insufflation when done at any time after a regular menstrual period the preponderance of pregnancies occurred after insufflation performed within the first two weeks after the period.

Summary.—Forty-nine out of the 59 cases becoming pregnant within a month after the insufflation were treated or examined by this method within two weeks after the period; 23 during the first week and 26 during the second week. In other words 87 per cent of the pregnancies followed insufflation when performed within two weeks while 13 per cent followed insufflation done later than two weeks after insufflation.

Although the therapeutic value of tubal insufflation is best judged by its immediate success as witnessed in the above 59 cases, it was interesting to compare the data in the 39 pregnancies which followed within two months after the insufflation. Of these 39 cases, 20 became pregnant who were examined by the method of insufflation within a week after the cessation of the last regular period; 14 cases within two weeks after the cessation of the last regular period; 2 cases the third week; 1 case twenty-six days; and 1 case six weeks after the last regular menstrual period. In one case the date of the last menstrual period was not definite. Here again it will be seen that the vast majority of pregnancies favored the insufflation done within the first two weeks postmenstruum (83 per cent).

Obviously the test cannot exercise any definite therapeutic value when more than two regular menstrual periods supervene. Here it simply has a diagnostic and prognostic value. The fact that eight women became pregnant after an interval of more than two years following the use of peruterine insufflation should cause us to pause in our prognosis before we give a hopeless outlook for childbearing when the fallopian tubes have been found to be patent. Doubtless there were other factors besides tubal that conspired to prevent these eight women from conceiving more promptly.

Summary of the 205 cases with respect to the tubal insufflation and the day following the last menstrual period.

84	were	done	during	the	first	week	postmenstruum.	
70	"	"	"	"	second	"	"	"
22	"	"	"	"	third	"	"	"
6	"	"	"	"	fourth	"	"	"
7	"	"	"	"	6 weeks to 7 months after the last regular period.			

1 was done a year after the last regular period.

In 15 cases the data regarding the last regular period are not given.

In 42 per cent of the 205 cases becoming pregnant the tubal insufflation was done within one week after the last period while in 75 per cent the insufflation was done within the first half of the menstrual interval.

Since the greater number of insufflations were done by preference in the first half of the menstrual interval than in the second half, it may well be argued that this fact in itself may account for the consequently greater incidence of pregnancy. But the results obtained for the one month and two month periods would still point to the postmenstrual phase as the best time for tubal insufflation to be done and as offering the best chance for impregnation. Other theoretic reasons for this preference were given in a special communication in the *Journal of American Medical Association*.[44]

The duration of marriage was recorded in 58 of the 59 patients who became pregnant one month after the test. In one case the exact duration of marriage was not recorded.

Twenty-two were married between one and three years; 17 were married for three to five years; 19 were married for five years or longer, of which 13 were married longer than five years.

Duration of marriage of patients who became pregnant two months after test is here summarized.

Nineteen were married between one and three years; 13 were married between three and five years; 7 were married longer than five years.

In other words 30 patients who were married three to five years at the time of treatment became pregnant within one or two months following tubal insufflation, and 26 patients who were married five years or over became pregnant within the first two months following the tubal insufflation. These figures give the impression more of post hoc ergo propter hoc than as favoring coincidence.

PERUTERINE TUBAL INSUFFLATION REPEATED AS A THERAPEUTIC MEASURE

A high initial pressure necessary to allow the gas to pass through the tubes and followed by pregnancy after insufflation may be assumed to point to its therapeutic value. In Douay's[5] series of 100 cases 18 became patent after repeated insufflation and 5 of these or 28 per cent became pregnant. Graff[10] found 44 per cent of his patients to have nonpatent or partially patent tubes. Twelve per cent of his cases became patent after repeated tests and of these (14 out of 43 cases) 32.6 per cent became pregnant.

Inasmuch as I am here dealing with the therapeutic side of peruterine tubal insufflation, the matter of its diagnostic value will not be entered into. A recent paper comparing it to intrauterine lipiodol injection deals with this phase.[45] It may be stated briefly that E. Graff found the results of the tube examination with peruterine insufflation to be corroborated in all of the 19 cases which were subjected to subsequent laparotomy.

A. Mandelstam[46] confirmed the findings by insufflation in 100 cases that came to operation. Mandelstam basing his conclusion upon 1500 pertubations states that "tubal insufflation is a safe and valuable procedure the use of which is not only desirable but indispensable in the treatment of sterility because it must be clear that without establishing the cause of the infertility no well founded therapeutic measure can and should be used." In 500 cases with positive results, that is where patency was demonstrated, Mandelstam was able to follow up results in 98 cases. Of these 98 cases 61 became pregnant; 4 the same month; 5 after two months; 3 after three months and the rest after four months to two and one-half years. In two cases with a negative pertubation result, pregnancy ensued.

Pertubation is considered by Mandelstam to be superior to salpingography although "in negative cases it gives no clue as to the site of obstruction." In cases of permeable tubes he does not use salpingography at all as a matter of principle and only employs the latter to diagnosticate the site of obstruction. Out of 34 cases of salpingography he met with 3 cases in which severe cramps followed the oil injection. By strictly observing the well-known contraindications he saw no complication in an uninterrupted series of 1200 cases although he had previously encountered 4 complications in his first 300 pertubations. In one case a skin emphysema was produced. In another case unilateral pyosalpinx and in two other cases an acute lighting up of gonorrheal adenitis. He is not content with attributing to the presence of such pathologic conditions as myomas, cystomas, infantilism, hypoplasia, conical cervix, hyperanteflexion of the uterus the cause of sterility in any case without first determining the patency of the tubes.

It will be recalled that George G. Ward[47] reported more than 3000 tubal insufflations from the special sterility clinic which he established at the Woman's Hospital. "In all that long series we have had no serious casualties. That, I think, shows that the test can be used with safety if proper precautions and care are taken."

Reynolds and Macomber themselves state: "Moreover, in the now considerable number of cases in which we have submitted the results obtained by this method to the test of operation we have so far met with no mistaken conclusion."

The cases in which the test was repeated once or twice may be said to be of particularly therapeutic value. The vast majority of these

repeated tests were done because there existed at the first insufflation some abnormality in tubal patency. In a few cases in which the insufflation findings were normal or practically normal it was repeated after coitus or before coitus intentionally for therapeutic reasons.

S. R. Meaker[15] reported three cases of women married and sterile for two, four and ten years respectively in whom pregnancy followed promptly upon the transuterine insufflation of gas. Two became pregnant immediately and the third became pregnant two months after the test. In each case considerable difficulty was encountered in forcing gas through the tubes. This was accomplished in the first attempt in two cases and at a fourth attempt in the third one. Meaker urges that insufflation should be tried as a routine therapeutic measure in all cases where every factor aside from the tubes has been excluded.

Cron[1] states that of 58 patients to whom he had sent questionnaires 14 reported pregnancy. The majority became pregnant after one or two months, some after a second inflation.

Guthmann[48] reports three pregnancies out of 15 cases who were examined by peruterine insufflation. Charbonnet[4] reports the case of a woman married six years who became pregnant following a second tubal insufflation in which the gas pressure rose to 180 mm. Hg. In the first attempt the pressure rose to 200 mm. Hg. Aldridge[3] reported nine cases of pregnancy out of his first series of 600 cases examined by peruterine insufflation. "Other cases may have occurred but no systematic inquiry had been made." Hirst and Mazer[12] reported three cases "who became pregnant so soon after the insufflation test that we are disinclined to view this phenomenon as incidental."

Geppert[9] in 1924 collected 30 observations of pregnancy in various publications following tubal insufflation. Marie von Scheller[20] in 1926 collected 59 among nine authors. Laurentie and Moussali[49] conclude that 7 undoubted cases of pregnancy have followed a short time after insufflation out of 550 cases examined. Serdukoff[50] reported 4 cases out of 64 insufflations. J. O. Polak in a private letter to Douay,[5] reported 5 cases of pregnancy out of about 100. Of 10 patients in whom the insufflation test was made at a pressure of 200 mm. Hg. the tubes originally closed were forced open by gas. One of these became pregnant. Another developed an ectopic pregnancy five months later. Rongy and Rosenfeld[51] have observed 3 cases of pregnancy after insufflation. Hugo Ehrenfest replying to a questionnaire submitted by Douay,[5] says that he has encountered a large number of pregnancies after insufflation, several after long standing sterility, proving that insufflation can overcome a tubal obstacle which prevents the passage of the ovum.

Summary of the manometric pressures in the 42 cases of my own series in which insufflation has been repeated follows:

There were 15 cases in which the gas pressure during insufflation was below 100 mm. Hg. on the first test.

There were 9 cases over 100 mm. Hg. and below 150 mm. Hg.
There were 6 cases between 150 mm. Hg. and 200 mm. Hg.
There were 10 cases at 200 mm. Hg.
There were 2 cases above 200 mm. Hg.

In 27 out of the 42 cases of pregnancy in which peruterine tubal insufflation was repeated one or more times the initial pressure reached before tubal patency was established was above 100 mm. Hg. The majority of the 42 had shown high grade stenosis to moderate stricture or spasm on the first or second test. The repeated test was carried out for diagnostic corroboration or therapy. In the future it will be well to bear this in mind. I have to confess to a certain timidity at first in employing the test for therapeutic purposes.

Seventy out of the 205 cases showed manometric pressures over 100 during tubal insufflation; of these 47 showed a pressure of 100 to 150; and 23 between 150 and 200; there were 135 cases in which the pressure was under 100 mm. Hg.

It is interesting to note that of the 15 cases out of the 42 in which the pressures were below 100, 6 belonged to the oligomenorrhea group and received x-ray therapy, the second insufflation following the x-ray therapy. In two other cases the insufflation was repeated after a myomectomy had been done. In two others the test was repeated after a child had been born following the first insufflation. These two patients gave birth to two children, conception having followed insufflation both times in each case. In one of these conception followed the same month. One of these insufflations was done for me by Dr. Harold Bailey.

TUBAL INSUFFLATION FOLLOWED BY LIPIODOL INJECTION

In two of the cases with the high pressures lipiodol was injected after the third test. In the one case after the third test, in the other the insufflation was repeated twice after the lipiodol injection before the patient became pregnant.*

PREGNANCY FOLLOWING SALPINGOLYSIS

In one case, a physician's wife, the insufflation showed kinked tubes at 200 mm. Hg. These were straightened out by laparotomy. Insufflation later proved them to remain patent at 110 mm. Hg. and she became pregnant soon after.

INSUFFLATION REPEATED AFTER IMPROVEMENT IN THE HUSBAND'S GENITAL CONDITION

In several of the normal patency cases the test was repeated after the husband improved under treatment from oligospermia to a normal spermatozoa production. In one of the latter the husband had a rela-

*It would be difficult to appraise the therapeutic efficacy of lipiodol injection in these two cases. But inasmuch as I have had occasion to inject lipiodol in 82 of the cases herein analyzed, and pregnancy followed insufflation and lipiodol injection in these two patients alone, the incidence points to a much greater therapeutic action on the part of the gas insufflation than the oil injection.

tively scanty output of spermatozoa because he gave up his blood for transfusions, and several months after he stopped being a blood donor his wife became pregnant.

INCOMPLETE TESTS

There were 4 cases in which one test was carried out and was considered incomplete. In one (Case 2) the cervical canal was found strictured; the uterine cavity was probably not entered but the patient promptly became pregnant. This case points to the rôle played by the stenosed cervix and the therapeutic effect of the cannula introduced into it. In one case a pressure of 200 was reached. The woman weighed 160 lbs., and as about 60 c.c. of gas was given, only the smallest part of it entered the peritoneal cavity through the strictured or spastic tubes. There was not enough to produce a visible subphrenic pneumoperitoneum or to occasion shoulder pains, and the patient was advised to have the test repeated. But this was not necesasry because she became pregnant that month. In another case the gas passed through freely at a lower pressure but not enough gas was introduced to produce the typical subphrenic pneumoperitoneum and shoulder pains. She became pregnant. In another case the first and only insufflation showed a pressure rise to 160 mm. Hg., and all the evidences of pateney were not present.

Where the fluoroscope fails to reveal a subphrenic pneumoperitoneum and the pressure is high, I have felt that the diagnosis of pateney should be held in abeyance till a second or a third insufflation can establish that fact.

In a fifth case with definite stricture of the tubes in a very obese woman, an ectopic pregnancy developed two years later. (Case 1 under ectopics.)

The second, third or fourth insufflation improved the tubal status in practically all of these 42 cases.

In 12 cases the pressures reached 200 mm. Hg. the first time and were within normal limits the second time.

In 5 cases they showed pateney with stenosis the second test, having proved closed or strictured the first time. One of these 5 cases proved to be normal on the third test, and in another case three tests were associated with a pressure of 200 mm. Hg. while the later 4 tests in the same case showed some pateney with the pressures ranging between 150 and 200 mm. Hg.

In 4 cases an initial spasm followed by pateney was encountered on the second test.

Although 200 mm. Hg. is the high limit of nonpateney as set down in my early work, increasing experience has taught that greater pressures may in some instances open up these tubes. Tubes that resist gas pressure up to 200 mm. Hg. on 3 tests may be said to be definitely

obstructed, yet it will perhaps occasionally happen that a fourth or fifth or sixth insufflation may overcome the obstruction.

The number of tests performed in these pregnancy cases totaled 261 as follows: once in 163 cases; twice in 34 cases; three times in 5 cases; four times in 2 cases; seven times in 1 case.

USE OF THE KYMOGRAPH

The value of the kymograph in these cases cannot be overestimated. Since May, 1925, it has been used in conjunction with tubal insufflation. It is particularly in connection with prognosis and therapy that it affords appreciable aid. Of the 205 cases becoming pregnant 161 were examined with the aid of the kymograph. In 44 cases the kymograph had not been used. Of the 161 cases there was evidence of uterotubalspasm in 5 cases; in 6 cases there was evidence of stricture, and in 9 cases high grade stenosis up to the high limit of closure, i.e., 200 mm. Hg. These cases required 3 tests, in one or two of which some degree of patency was noted.

Thanks to increased experience gained through the aid of the kymograph it has been possible to repeat the test with greater intelligence on the one hand and with more gratifying results on the other.

PRECAUTIONS AGAINST CONCEPTION

In 89 cases no statement as to precautions was made (earlier cases of the series).

In 116 there were data as to precautions against conception.

Seventy-seven took precautions. Of these 77 who took precautions at some time, 67 stopped contraceptive measures for a period of from one to three years; 8 for a period of from three to five years and 2 for a period of from five to seven years.

Thirty-nine did not take precautions. Of these 39, 15 were married for a period of from one to three years; 15 for a period of from three to five years; 7 for a period of from five to seven years; 1 for twelve years and 1 for fourteen years.

The laity is so far educated along these lines that it requires very little persuasion to get married couples, elderly at the time of marriage, to avoid taking any precautions against conception because they realize the short time left to demonstrate their power to reproduce. The reasons for the relatively lowered fertility are to be found in the occasional definite profound changes in constitutional and local regional viscera; e.g., chronic congestions; mental and physical fatigue; vices in diet and rest and exercise; intercurrent diseases, etc.

How does uterotubal insufflation aid the sterile woman?

Peterson and Cron[1] commenting on the therapeutic application of the test from their own experience state that "something more than the mere passage of the gas and the mechanical opening of the tubes

must be considered in trying to explain the higher percentage of pregnancies in those women who had previously conceived (4 out of 6, as against 9 out of 30 primary sterilities)." Although my series shows a reversal of their results (73 out of 930 secondary sterilities; whereas 132 out of 1070 primary sterilities became pregnant), the fact remains that the exact mechanism by which tubal insufflation aids the sterile woman cannot be explained in a certain number of cases.

For the majority of successful results I ventured in 1925[24] to state four ways by which tubal insufflation may act as a therapeutic measure in female sterility.

1. By establishing patency of the genital tract from the external os to the abdominal opening of the Fallopian tubes. Any cervical canal that is patulous to the uterine cannula used in the uterine insufflation is ample for the entrance of spermatozoa. If the external os appears punctate or pinpoint but admits the cannula, this is proof that it is wide enough to allow semen to enter the cervical canal. The cannula at the same time stretches it somewhat, rendering it more patent for a varying period of time. Should coitus take place shortly after this procedure, the spermatozoa must have a better opportunity to enter the uterine cavity.

2. In some cases a mucous plug not visible at the external os but occupying the deeper portion of the cervical canal is expelled after the insufflation and on withdrawal of the uterine cannula. I have the impression that the removal of this mucous plug in this manner may be the important factor in some of the successful cases.

3. By separating mild agglutinations of the folds of the tubal mucosa, by straightening out tortuous tubes, especially of the infantile type, by dislodging a mucous inspissation from a narrow to a wider portion of the tube, by actually separating adhesions at the fimbriated end in cases requiring 150 to 200 mm. Hg. or more, a way is opened for the descending ovum to meet the ascending spermatozoa.

4. Still another factor not to be lost sight of is the psychic impression which peruterine insufflation makes on the patient. Although the exact nervous mechanism is not at present clear, there are women who respond to the physical stimulation of peruterine insufflation through the psyche acting upon the autonomic genital apparatus. Whether it induces a certain amount of relaxation in otherwise spastic tubes, the uterine openings of which are practically closed, must await further inquiry.

That there actually exists in certain tubes spasm sufficient to close the uterine ostium in a manner similar to the closure of the internal os of the uterus has been recently demonstrated. I have been able to convince myself of the presence of spasm in about 4 to 5 per cent of cases and believe that it is very common in the premenstrual interval. Overcoming such spasm may obviously exert a therapeutic influence.

STERILITY AS A SOCIAL WELFARE PROBLEM

Giles[26] regards sterility as an expression of a lowered standard of health, and therefore considers it a matter "for considerations of public welfare and also a loss to the nation of unborn children." "It is evident," says he, "that with the limitation of the number of marriages it is increasingly important that the marriages that are consummated should be fruitful."

"If," says Batuaud,[52] "each medical man in France could restore eight sterile marriages the problem of the population of France would be solved." So that any measure which promotes the general propagation of the species may be welcome.

GENERAL SUMMARY

1. There were 1070 primary sterilities and 930 secondary sterilities. One hundred thirty-two cases of primary sterility became pregnant, and 73 cases of secondary sterility became pregnant.

2. A history of induced and spontaneous abortion was given by 49 patients of the 73 secondary sterilities out of the 205 who became pregnant following tubal insufflation or an incidence of 67 per cent of the secondary sterilities, 31 patients with 38 spontaneous abortions and 18 patients with 26 induced abortions.

3. In 85 of the cases some surgical operation was noted in the history. In 120 no operation was recorded.

4. One hundred eighty-eight had full-term children; 17 had early miscarriages, or 8.3 per cent of the total 205 cases.

5. There were 3 additional pregnancies out of the 2000 cases which resulted in ectopic pregnancy, or one in 666 cases.

6. There were 54 women over thirty years of age, or 27 per cent of the total number who became pregnant.

7. Fifty-nine pregnancies occurred within one month after insufflation and 39 within the second month making a total of 98 cases of pregnancy following insufflation within the first two months or nearly 50 per cent of the cases.

8. Of the 73 relative sterilities 38 had failed to become pregnant for three years following the last full-term pregnancy or abortion; 17 for five years; 11 for seven years; 5 between seven and ten years; and 2 for longer than ten years (1 for twelve years and 1 for fourteen years).

9. In 92 of the 205 cases some adjuvant treatment was resorted to. In 113 cases no other treatment than tubal insufflation was given. The cases that promptly became pregnant were not those receiving gland extracts.

10. In all cases where a pressure of 200 mm. Hg. has been reached the possible occurrence of ectopic pregnancy must be borne in mind.

11. In 154 cases the insufflation was done between the first and the fourteenth day following the cessation of the last period; i.e., in the

preovular phase. This would point to the first half of the menstrual interval as being the more favorable for therapeutic tubal insufflation. This is particularly noted in the 59 cases which became pregnant within one month after the insufflation, 24 of which were insufflated within seven days from the last menstrual period and 25 the second week after the last menstrual period. In other words 87 per cent of these 59 pregnancies followed insufflation when performed within two weeks while 13 per cent followed insufflation done later than two weeks postmenstruum. In 83 per cent of the 49 patients who became pregnant within two months after the last regular period, the insufflation had been done within the first two weeks postmenstruum.

12. Thirty patients who were married from three to five years at the time of treatment became pregnant within one or two months following insufflation; and 26 patients who were married five years or over became pregnant within the first two months following insufflation. This is the best evidence of the therapeutic efficacy of the test.

13. Of the 205 cases becoming pregnant insufflation was done in 42 per cent within one week after the last period and in 75 per cent within the first two weeks after menstruation.

14. In 27 of the 42 cases of pregnancy in which peruterine insufflation was repeated one or more times, the initial pressure reached before tubal patency became established was above 100 mm. Hg. In 12 cases the pressure reached 200 mm. Hg. the first time and within normal limits the second time. Although 200 mm. Hg. is the high limit of nonpatency as set down in my early work, increasing experience has taught that greater pressures may in some instances open these tubes. Tubes that resist gas pressure up to 200 mm. Hg. on three tests may be said to be definitely obstructed. Yet it will perhaps occasionally happen that a fourth, fifth or sixth insufflation may overcome the obstruction.

15. Of 116 cases with definite data as to precautions against conception there were 77 patients who took precautions and 39 who did not take precautions. Of the 77, 67 had taken no precautions for a period of one to three years; 8 for a period of three to five years; and 2 for a period of five to eight years. Of the 39 who did not take precautions, 15 were married for a period of one to three years; 15 for a period of three to five years; 7 for a period of five to eight years; one for twelve years and one for fourteen years.

CONCLUSIONS

That there is a definite therapeutic efficacy of the method may be concluded from the cases in which pregnancy followed tubal insufflation within a month in women over thirty years of age and who were married for a period of five years or more, no treatment other than insufflation having been used and no contraceptive precautions taken

for at least a year. Furthermore the cases in which the initial pressure was high on the first insufflation or was reduced to a relatively normal level by a repeated test just before pregnancy took place also indicate a therapeutic action on the part of the insufflation and thus eliminate the possibility of chance or accidental results.

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911 PARK AVENUE.

RADIUM IN THE TREATMENT OF MENORRHAGIA OF ADOLESCENCE AND OF THE MENOPAUSE*

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PREVIOUS to 1832 many bizarre theories were advanced regarding the function of menstruation. In 1832 Negrier discovered that the ovary was related to the occurrence of menstruation and in 1840 Gendren brought forth the theory that menstruation depended on ovulation. Later Pflüger's theory was accepted that menstruation occurred as a result of irritation of the ovarian nerve caused by the distention of the ovary as a result of the swelling of the follicles. This reflex irritation in turn was supposed to dilate the utero-ovarian arteries and so produce pelvic congestion and uterine bleeding. This theory was accepted until Marshall, Jolly and others showed that menstruation persisted following transplantation of the ovaries, establishing the fact that the ovaries were responsible for menstruation and that the stimulating substance must travel by way of the blood stream. This observation led to the work of Papanicolaou, Stockard and Frank and later to that of Allen, Doisy and others, which in turn led to the now accepted hormone theory.

The menorrhagia and metrorrhagia of adolescence and of the menopause in which a demonstrable pathologic lesion is not present would seem to be due to ovarian dysfunction, especially in the former period. In menorrhagia of the menopause other factors, such as repeated preg-

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nancies, low-grade chronic endometritis, hypertension, or fibrosis of the uterine muscle may play a part. The effect of the beta and gamma rays of radium on the endometrium and on the ovarian follicles has established radium as a valuable adjunct in the control of uterine bleeding. In this study only the histories of those patients treated with radium in whom pelvic lesions were not found were selected.

Perhaps the policy in The Mayo Clinic may have been overly cautious in the use of radium in the management of menorrhagia and metrorrhagia of adolescence. Radium has been used in these cases only when all medical measures have failed to control the loss of blood and when the persistent anemia or the incapacity of the patient necessitated more radical treatment. Fifteen unmarried patients between the ages of fourteen and twenty-one were given radium for menorrhagia from 1916 to 1927 inclusive. In 7, menstruation had been irregular since its onset; in one, the periods were regular but prolonged and in 7 the periods had been irregular for from one to four years, the flow in 3 having been continuous for more than six months. The onset of menstruation was somewhat delayed; in 4 patients, the catamenia occurred at the age of fifteen and in 5 at the age of fourteen; menstruation was established at the age of thirteen in 4 and at twelve years in 2.

It is perhaps significant, in view of the endocrine theory, that only 2 of these girls were overweight, between 145 and 150 pounds, in contrast to the large proportion of girls having scant menstruation or amenorrhea who are overweight. Six of the girls weighed less than 110 pounds and 6 weighed between 110 and 125 pounds. The weight of one was not mentioned. In most of the cases treatment for menorrhagia had been given without permanent benefit before radium was used. In 6 cases treatment by glandular extract had been more or less consistent. In 11 cases the uterus had been curetted; in one the uterine ligaments had been shortened; in 2 hysterotomy had been performed; in one case immediately preceding, and in one nine months previous to the application of radium. In one case a polyp had been removed a year previously and in one an ovarian cyst had been punctured during operation for appendicitis. In all of the cases menorrhagia or metrorrhagia had recurred. On bimanual examination, the uterus was found to be in the usual anterior position in 11 cases and retroverted in 4; the organ was considered to be of normal size in all but one case, in which the size of the uterus was graded 3. Abdominal hysterotomy was performed in this case but only extensive polypoid endometritis was found. In 2 cases the ovaries were found to be enlarged on bimanual examination.

The loss of a moderate amount of blood or even a slight amount over a long period of time often produces more marked secondary anemia than the loss of large amounts of blood at fairly long intervals. In 5 cases, the hemoglobin was below 40 per cent and in 3 it was between 50 and 60 per cent; 2 patients were given a transfusion previous to the

use of radium. Transfusion may control menorrhagia of this type but these 2 patients had come a long distance and the hemorrhage had lasted so long that it did not seem advisable to rely on transfusion alone.

The amount of radium used varied from 100 to 700 mg. hours. Three patients received 100 mg. hours, five 150, four 200, one 300, one 520, and one 700.

In the small group of adolescent cases, the results were not uniform and it would seem impossible to determine a uniform dosage. One patient was given 150 mg. hours, without improvement, and another who received the same amount ceased menstruating for three years. The results are shown in Table I.

One patient improved for six months, then the menorrhagia and metrorrhagia returned, increasing in severity, and the uterus became large and soft. Hysterectomy was performed three years after the application of 100 mg. hours of radium and the pathologic diagnosis was carcinoma of the fundus. This patient is well nine years after the operation. Hysterectomy was performed elsewhere on one patient three years after 150 mg. hours of radium had been given. In two cases, radium was repeated. One patient received 340 mg. hours three years after the initial dose of 100 mg. hours and the periods then became normal. The other patient, after receiving 150 mg. hours, returned a year later and was given 225 mg. hours; she has reported that menstruation is normal but less frequent. One patient receiving 200 mg. hours improved for one year, then the profuse flow returned, following which exploratory hysterotomy was performed, the ligaments shortened and a cyst of the ovary punctured. The periods are now irregular but less profuse. One patient who received 520 mg. hours of radium did not menstruate for six months, then menstruated once, the period lasting three weeks. Further report has not been received from this patient. One patient who received 125 mg. hours has scant menstrual flow every six weeks. One patient who received 150 mg. hours did not menstruate for three years, then began to flow profusely and a pelvic operation (nature unknown) was performed elsewhere. One patient who received 200 mg. hours of radium reported improvement; another patient given 700 mg. hours menstruated twice normally, then the flow became profuse and radium was applied to the spleen. The menorrhagia was not controlled. Operation (nature unknown) was performed elsewhere two years later. The menstrual periods of four patients became regular and normal; two of these received 150 mg. hours each, one 300 mg. hours and one 200 mg. hours.

During or near the menopause conservation of ovarian function may be disregarded and sufficient radium can be given to produce permanent cessation of menstruation. It is in this group that radium gives the most satisfactory results in controlling the menorrhagia. The one

TABLE I. THE APPLICATION OF RADIUM DURING ADOLESCENCE

CASE	AGE	MILLIGRAM HOURS	PREVIOUS TREATMENT	RESULT
1	17	100	Thyroid extract, iron, rest.	Improved for six months, then gradually increasing metrorrhagia; abdominal hysterectomy three years later; carcinoma of fundus; well now nine years after hysterectomy.
2	18	100	Corpus luteum with temporary improvement.	No change; three years later 340 mg. hours; periods normal since; gained strength and weight.
3	18	150	Corpus luteum with some improvement; curettage one year before and preliminary to radium.	Return of profuse flow after treatment; hysterectomy elsewhere three years later.
4	19	200	Short treatment with corpus luteum; curettage two years before and preliminary to radium.	Improved one year; profuse flow returned; gained 17 pounds, exploratory hysterotomy; ligaments shortened; ovarian cyst punctured; periods improved but still irregular.
5	18	520	Ligaments shortened; curettage two years and one year before.	Periods ceased for six months, then one period of three weeks' duration; no report since.
6	17	200	Curettage two years before; hysterotomy; curettage and rupture of ovarian cyst preliminary to radium.	No report.
7	18	125	Ovarian extract for six weeks; curettage eight months before and preliminary to radium.	Small amount of flow every six weeks; general health fair.
8	20	200	Curettage; removal polyp one year before; roentgen ray for one year; no benefit.	Some improvement.
9	16	150	Curettage two years and one year before; hysterotomy preliminary to radium.	Flow ceased after two weeks for three years; returned profuse; pelvic operation elsewhere (nature unknown) three years later; gained strength but not weight.
10	19	150 (225 1 year later)	Mammary gland extract; curettage five months before and preliminary to radium.	Flow stopped for a time, then re-established but periods far apart; gained strength and weight.
11	19	700	Curettage one year, and again six months before.	Two normal periods then profuse again; radium to spleen without benefit; operation elsewhere two years later; improved since.
12	15	150	Curettage one year before without relief.	Periods ceased six months, then regular and normal; gained strength but not weight
13	18	150	None recorded.	Periods every six to seven weeks for five to six days; gained weight.
14	20	300	Curettage preliminary to radium.	Periods regular and normal; gained weight.
15	20	200	Ovarian tablets for four months.	Periods regular and normal; gained strength.

definite contraindication to its use is the history or local evidence of previous pelvic infection.

During the years 1920 to 1924 inclusive, 284 women, in whom fibromyomas were not detected by examination, were treated at The Mayo Clinic for menorrhagia during the menopause. The average age of these women was forty-five and seven-tenths years; 54 were between fifty and sixty. Of the 270 married women, pregnancy had occurred in 251 (92.96 per cent); 239 (95.21 per cent) of these had had children. Nineteen (7.03 per cent) of the married women had not been pregnant and twelve (4.76 per cent) had had miscarriages and full-term pregnancies had not occurred. There was one ectopic pregnancy. Although there may not be an etiologic relationship with intercurrent infection 100 (35.21 per cent) of the patients had had influenza.

TABLE II. AMOUNT OF RADIUM USED AND RESULT OF TREATMENT

RESULT OF TREATMENT	RADIUM IN MILLIGRAM HOURS												TOTAL
	250-450		500-750		800		1000		1200		1400-1500		
	PATIENTS	PER CENT	PATIENTS	PER CENT	PATIENTS	PER CENT	PATIENTS	PER CENT	PATIENTS	PER CENT	PATIENTS	PER CENT	
Periods ceased immediately	3	37.5	98	80.9	11	91.6	10	90.9	57	91.9	28	93.3	207
Periods irregular, amount normal	2	25.0	13	10.7	1	8.3	1	9.0	2	3.2	1	3.3	20
Periods irregular and profuse	2	25.0	5	4.1					1	1.6			8
Normal periods	1	12.5	2	1.6							1	3.3	4
Second radium treatment required			2	1.6									2
Hysterectomy performed later			1	0.8					2	3.2			3
Total	8		121		12		11		62		30		244

Prolonged and profuse menstruation had occurred in 188 cases (66.19 per cent), in 33 (11.61 per cent) bleeding had been continuous, and in 162 (57.04 per cent) the periods were irregular. Curettage performed previously had failed to relieve the menorrhagia in 55 cases and in 124 curettage for diagnosis was performed preliminary to the use of radium. In two cases myomectomy had been performed and in one case partial hysterectomy for fibromyomas. In 6 cases, intrauterine polyps had been removed. One ovary was removed in one case and in 9 cases partial oöphorectomy was performed.

In the group of patients who were passing through the menopause, 207 (of the 244 heard from) ceased menstruating immediately following the use of radium. Twenty patients menstruated irregularly but profusely and four menstruated normally. Two patients were given second doses of radium. Hysterectomy was performed on three patients because of recurrence of symptoms.

In the group of 8 patients given 250 to 450 mg. hours of radium, 3 ceased to menstruate immediately, 2 menstruated normally but irregularly, 2 menstruated irregularly and profusely, and one menstruated normally.

In the group of 121 patients given 500 to 750 mg. hours of radium, 98 ceased to menstruate immediately; 2 again menstruated normally; 5 experienced a return of profuse menstruation, 2 of whom were given subsequent applications of radium, one, one year later and one, nine months later and then ceased menstruating. Thirteen menstruated irregularly from two to seven years and then menstruation ceased. Two of these patients died, one from pernicious anemia and one from pneumonia; hysterectomy was performed one year later on one patient and a pathologic diagnosis was made of a malignant lesion in the fundus.

In the group of 12 patients given 800 mg. hours of radium, 11 ceased to menstruate immediately; one patient menstruated irregularly but less profusely, and reports have not been received from 2 patients.

In the group of 11 patients given 1000 mg. hours of radium, 10 ceased to menstruate immediately; one of these patients died from embolus following an operation for bunions elsewhere two years later; one menstruated irregularly, and reports were not received from 5 patients.

In the group of 62 patients receiving 1200 mg. hours of radium, 57 ceased menstruating immediately; one of these died three years later from apoplexy. Hysterectomy was performed elsewhere on one patient for hemorrhage three years later; 2 patients menstruated irregularly; one patient menstruated profusely and irregularly for five years and then menstruation ceased. Reports were not received from 13 patients.

In the group of 30 receiving 1400 mg. hours of radium, 28 ceased menstruating immediately, one patient menstruated irregularly for a year and then menstruation ceased, and one patient menstruated normally.

Two patients received 1600 mg. hours of radium. One ceased to menstruate immediately; a report was not received from the other.

CONCLUSIONS

1. In the adolescent period, radium should not be used until after all general and other accepted measures of treatment have failed. The dose should be small enough to preclude any possible injury to the ovary. It is better to err on the safe side and repeat the dose several months later if necessary than to use a dose which might permanently injure the ovarian tissue. Although it is hard to establish a definite dosage, we believe that not more than 200 to 250 mg. hours should be used in the initial treatment.

2. It is evident that the use of radium is of distinct value in controlling menorrhagia of the menopause.

3. From 800 to 1000 mg. hours of intrauterine radium in a single dose gives satisfactory results in more than 90 per cent of patients treated.

4. The history of pelvic infection even eight or ten years previously or evidence of pelvic infection is a definite contraindication to the use of radium.

5. Preliminary curettage for diagnostic purposes should be carried out in practically all cases in which the patient is more than forty years of age.

THE RADIUM TREATMENT OF FIBROIDS AND FIBROSIS UTERI*

By Frederick A. Cleland, B.A., M.B., F.A.C.S., Toronto, Canada

IT IS thirty years since the discovery of radium and twenty-eight since Walkhoff first recorded the reaction produced on human tissues by this peculiar element. Robert Abbè says he treated fibroids with radium as early as 1905, but the first report of its action on uterine fibromas and chronic metritis was made in 1906 by Oudin and Verchère. The pioneer work in America was done largely by Kelly and Burnam, Clark, and Norris and Keene. Many others have confirmed the results of their observations and certainly enough work has been done in the last fifteen or twenty years to warrant us making very definite conclusions as to the value of radium to the gynecologist. In the treatment of certain conditions the use of radium is now upon a firm foundation and early prejudices are no longer justifiable.

When our president asked me to take the subject of radium in the treatment of fibroids, and I began to examine my records, I felt that it would give a wrong impression were I to confine my observations only to the treatment of uteri in which definite fibroids could be demonstrated, leaving out those cases in which radium is especially applicable, that is, the bleeding and enlarged uteri where no nodule is present, the so-called fibrosis uteri. Therefore, in presenting a series of two hundred cases treated by radium from January 1, 1922, to December 31, 1927, I have divided them into two classes, namely, fibroids and fibrosis uteri. The term fibrosis uteri is, perhaps, not an ideal one but it seems to be the best at hand and that most commonly used in America. I believe it was first used by Bland-Sutton in 1899 in defining chronic metritis or fibrosis uteri, in which the leading feature is menorrhagia, which cannot be controlled by drugs, tampons, or curettage. He described these uteri as presenting striking structural changes, the organ being larger than usual and walls thick and tough. Other writ-

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ers before Bland-Sutton have described chronic metritis and subinvolution but as far as I know none of them used the words fibrosis uteri. Since then many investigators, including Findley, Gardner and Goodall, Shaw, Donald, Rabinovitz, Novak, Geist and Scott, have made contributions to the literature regarding the etiology of this condition. It must be admitted that the etiology is not yet settled and that no definite pathologic findings are constantly present. I choose to use the name of fibrosis uteri as a clinical term rather than a pathologic entity. In every case which I am reporting as fibrosis uteri, the uterus was definitely enlarged, having thick dense walls and no nodule. I have excluded all cases of idiopathic or myopathic bleeding in which the uterus did not show enlargement.

In the tables given the cases are entirely from private records. It was found impossible to investigate and follow up public hospital cases with sufficient accuracy, and we gave up the attempt. The 207 cases treated surgically are also from private records, and include all cases of fibroids operated upon during the same period.

In the 200 cases treated by radium the technic was practically uniform. The cervix was dilated and a diagnostic curettage done, after which the uterine cavity was wiped out with gauze. The radium needles were screened with 1 mm. of brass and 1.6 mm. of gray rubber tubing, and accurately placed in the uterine cavity and held securely in position by a catgut suture through the cervix and rubber tubing, or by plain gauze packing. If sutured in position, a full length catgut suture was used, and tied by a slip knot, easily loosened when the radium was removed.

Table I shows age incidence and is made in conformity with that of other writers. It shows 50 patients under forty years of age; but of these, 22 were over thirty-eight years. It is a point worth noting therefore that over two-thirds of all our cases were between the ages of thirty-eight and fifty.

TABLE I

AGES	NO. OF PATIENTS	MENOPAUSE INDUCED IN
20 - 30	9	3
30 - 40	43	25
40 - 50	117	113
50 - 60	26	25
60 - 70	5	Menopause before radiation
Total	200	

Of these 200 cases 98 were diagnosed as fibrosis uteri.

FIBROSIS UTERI CASES

In all of these patients the uterus was larger and denser than normal. The 98 patients were distributed according to ages as follows, and Table II also shows the number of patients in whom the menopause was induced.

Only 15 of these were under thirty-eight years of age. Of the 98 patients 13 or about 14 per cent were unmarried. Many of the married patients had had a number of children, as is shown in Table III, and probably subinvolution was an etiologic factor.

TABLE II

AGES	NO. OF PATIENTS	NO. OF PATIENTS IN WHOM MENOPAUSE WAS INDUCED
20 - 30	5	1
30 - 40	22	15
40 - 50	54	52
50 - 60	14	14
60 - 70	3	Menopause previous to treatment
Total	98	

TABLE III

	0 CHILDREN 0 MISCARRIAGES	MISCARRIAGES ONLY	1 CHILD	TWO CHILDREN	3 TO 5 CHILDREN	MORE THAN 6 CHILDREN
No. of patients	6	4	8	20	35	7

The family history of 5 patients was unknown. Seventy-seven per cent of the married patients whose family history was known had had 2 or more children.

Twenty-two of the 76 married patients whose family history was known had had one or more miscarriages. The 15 patients under thirty-eight years are discussed elsewhere. In *all* the older patients of this group, the results were successful. The majority of the patients received doses of from 1200 to 1500 mg. hours. In a few patients where the uterus was particularly large, as much as 1700 to 1900 mg. hours were given. In all but one of these patients the menopause was induced. In this one exception the excessive bleeding was controlled and normal menstruation followed. One application of radium was 100 per cent successful in these 83 patients over thirty-eight years of age, nearly all of whom had had several children, and were suffering from marked menorrhagia.

FIBROID CASES

Many of the fibroids were small, but many were intramural as large as a three months' pregnancy. A few larger than a three and a half months' pregnancy gave good results, but as a rule it is considered that tumors of that size are better treated by surgical removal. The distribution of these cases according to age as shown in Table IV does not differ markedly from that shown by the fibrosis uteri cases.

Only 13 of these were under thirty-eight years of age. Of the 102 patients, 17 were unmarried. Many of the married patients had had

large families, only eight had had no pregnancies, and 65 per cent had had more than two children, not as high a percentage as that among the fibrosis uteri cases.

TABLE IV

AGES	NO. OF PATIENTS	NO. OF PATIENTS IN WHOM MENOPAUSE WAS INDUCED
20 - 30	4	2
30 - 40	21	8
40 - 50	63	61
50 - 60	12	10
60 - 70	2	Menopause previous to radium
Total	102	

TABLE V

	0 CHILDREN 0 MISCARRIAGES	MISCARRIAGES ONLY	1 CHILD	TWO CHILDREN	3 TO 5 CHILDREN	MORE THAN 6 CHILDREN
No. of patients	8	3	18	21	25	7

The family history of three patients was unknown. Twenty-nine, or 35 per cent of the 82 married patients whose family history was known, had had miscarriages, a normal percentage probably. Lockyer and others have found that sterility is twice as common among married women with fibroids as among married women without these growths. Also the risk of abortion is much increased. Our figures did not confirm his findings.

With these cases the proper dosage was more difficult to gauge, but it varied with the size of the tumor. We aimed to bring on the menopause, as this seemed to be necessary for effective treatment. Most of the patients received a little more than the fibrosis cases, usually about 1400 to 1500 mg. hours. A few were given 1200 mg. hours, and a few others received from 1900 to 2100 mg. hours. One whose uterus was the size of a four and one-half months' pregnancy received 3680 mg. hours with satisfactory result. As a rule patients around thirty-eight to forty years need larger doses to induce the menopause than those nearer their natural climacterium; at that time a very small dosage may be sufficient.

Unsuccessful Results.—In nine of these patients the treatment was unsuccessful, and in seven, hysterectomy was performed without mortality, four by other surgeons and three by myself. In most of these cases the reason for the poor result was later evident. (See Table VI.) In two patients the fibroid underwent degeneration, as examination after removal proved. Another had a submucous fibroid about the size of a small walnut, which was not detected at the time the radium was used. Two were underradiated. In the sixth patient the tumor rapidly increased in size and caused death three months after radia-

tion. It was probably sarcoma, although the scrapings were negative; no further operation was done and no postmortem allowed. The seventh patient, a woman of sixty-two years, weighing over 250 pounds, had a very large fibroid extending half way to the umbilicus. This tumor was probably too large for radiation, but as the bleeding was never profuse, the patient did not want any further treatment. In the remaining two cases no reason for the failure was known.

TABLE VI

	DEGENERATING FIBROIDS	SUBMUCOUS	UNDERRADIATION	UNDIAGNOSED MALIGNANCY	TOO LARGE	NO KNOWN CAUSE
No. of patients	2	1	2	1	1	2

The patients under thirty-eight years of age should be discussed as a group by themselves, as in many instances it was our aim to control the excessive bleeding, always the main symptom, without stopping the menses permanently. As the menorrhagia had been of long duration, the menopause was brought on in ten of these twenty-eight patients, all intentionally, excepting one. These patients received 900 to 1500 mg. hours. In the remaining 18 patients, doses varying from 500 to 1500 mg. hours caused amenorrhea for from two to twelve months. In only one was treatment ineffectual. This patient, aged twenty-five, a case of fibrosis uteri, had no periods for three months after 900 mg. hours, but then bled severely again. Further radiation was advised but disregarded.

Doses up to 900 mg. hours apparently can be given with safety and half of these women were successfully treated with doses varying from 1000 to 1500 mg. hours. Three of these patients or 10 per cent subsequently became pregnant, two of whom gave birth to living children.

SYMPTOMS BEFORE AND AFTER RADIATION

1. *Bleeding.*—All of the 200 women except three complained of abnormal bleeding, usually beginning as a menorrhagia but frequently becoming almost continuous. A few had bleeding come on after menopause. Of the three who had no unusual bleeding, one had had frequent miscarriages, and a fibroid so low that myomectomy was considered impossible; the other two complained only of abdominal discomfort and were exceedingly poor operative risks because of myocardial disease. In 95 per cent of the patients the bleeding was controlled by one application of radium. The patients had to be warned that the radium took some time to accomplish its work and two or three menstrual periods might come on before the desired result was established. Table VII shows the number of menstrual periods that the women in this series had after radiation.

More than half of the patients had no bleeding after radiation. If the treatment is given shortly after the last period there is less likeli-

hood of the next menses coming on. If it is applied a few days before a period the next flow is apt to be particularly profuse.

TABLE VII. MENSES AFTER RADIATION BEFORE ALL BLEEDING STOPPED

	NONE	1 PERIOD	2 PERIODS	3 OR 4 PERIODS	12 TO 18 PERIODS
No. of patients	103	34	18	10	4

2. *Climacteric Symptoms.*—In the questionnaires that were sent to the patients, they were asked if they had had hot flushes and if so how severe these had been. This climacteric symptom was chosen because it is probably the most constant and the most easily described. Undoubtedly the patient's estimate of the severity of her symptoms depends considerably on her temperament. The answers to this question are summarized in Table VIII.

TABLE VIII. HOT FLUSHES IN ALL THE PATIENTS IN WHOM THE MENOPAUSE WAS BROUGHT ON

	NONE	MILD	SEVERE	NOT DESCRIBED
No. of patients	31	73	58	4

Even at the natural menopause great variation in the symptoms occurs, and it is not felt that these results were at all abnormal. Danforth came to the same conclusion. Stevens and Weiss claim that the symptoms are less severe than those seen at the normal menopause.

3. *Leucorrhea.*—In the whole series 84 complained of leucorrhea before they were radiated. In describing this symptom there is also a great personal variation. On examination 162 showed definite signs of endocervicitis, and in all of these the cervix was cauterized after dilatation. That this treatment is successful is evidenced by the fact that only 31 had any discharge after it and in two-thirds of these, this lasted but a few weeks. Six months or more elapsed before the watery discharge disappeared in the other ten.

4. *Pain.*—None of these patients complained of pain. Pain other than dysmenorrhea is a contraindication to the use of radium. Three young patients who suffered from marked menstrual pain were relieved of this symptom when the menses returned following the temporary amenorrhea. Naturally those in whom the menopause was induced suffered from this symptom no longer.

REDUCTION IN SIZE OF TUMORS OR THE UTERUS

Only in a comparatively few of the cases (30) were bimanual examinations made after the radiation. In all but four of these the uterus or the fibroid was considerably smaller even after as short a period as two months. In two cases where the uterus did not decrease in size

the finding was of importance. In these patients after some months, the fibroid was found to be degenerating and hysterectomy had to be performed.

COMPLICATIONS

One patient developed pelvic cellulitis with severe pain two weeks after treatment, which necessitated six weeks longer in hospital. A second had a severe pyelitis three days after radiation, which prolonged her stay in hospital about two weeks.

MORTALITY AND MORBIDITY AS COMPARED WITH SURGERY

In the 200 cases there was one death, and this occurred from an embolus on the ninth day after radiation. The patient was a large woman weighing about 190 pounds, very anemic and her uterus was about as large as a three and a half months' pregnancy, with several distinct fibroids posteriorly. It was felt that the tumor was about the largest size possible for radiation, but as she was a poor surgical risk, radium should be tried first.

During the same six years the following operations were performed for fibroids:

TABLE IX

TYPE OF OPERATION	NO. OF PATIENTS	NO. DEATHS	PER CENT DEATHS
Supravaginal Hysterectomy	153	5	3.3
Total Hysterectomy	29	0	0.0
Myomectomy	25	0	0.0
Total	207	5	2.4

One should remember, however, that the more dangerous types of fibroids, for example those undergoing degeneration, can only be treated by surgical removal and these naturally raise the mortality rate.

We have no definite figures on the comparative morbidity of radium and surgery, but whereas hysterectomy or myomectomy means two to three weeks in the hospital, radium treatment after dilatation, diagnostic curettage, and cauterization mean only four or five days with no special nursing required.

CONTRAINDICATIONS TO RADIUM

1. Fibroids larger in size than a three and a half months' pregnancy are considered unsuitable for radiation. A fibroid which is causing pressure symptoms such as urinary frequency, difficulty in defecation or unilateral edema of the leg should not be treated with radium.

2. The presence of adnexal disease or ovarian tumor prohibits the use of radium. Some gynecologists refuse to use radium in any individual who gives any history of previous adnexal disease, even though it may have occurred many years previously, but this seems to be excessively cautious. Provided there is no tenderness and no palpable masses are present one may proceed with the treatment.

3. Any symptom which suggests that the fibroid is undergoing degeneration should warn one not to use radium, for example, soft, rapidly enlarging or tender tumors, especially if associated with slight fever and leucocytosis. Pain is usually a symptom of degeneration. Fibroids which have become calcareous are not benefited by radiation. Secondary anemia more marked than that due to the loss of blood is usually indicative of degeneration.

4. Subperitoneal fibroids are usually not suitable and may be caused to degenerate by such treatment, because of fibrosis of the pedicle with subsequent reduction of the blood supply. Submucous fibroids are also better treated surgically.

5. If there is any uncertainty of diagnosis the tumor should be investigated surgically.

6. In young women myomectomy if possible should be done in preference to radiation.

7. If there is any coincident pathologic condition in the abdomen which requires operative treatment, the entire operation should be carried out surgically and not combined with radium.

The value of any therapeutic agent is determined by its end-results. While one is undoubtedly influenced by the opinion of others, one's own experience must be the best and safest guide, and my conclusions are drawn from my own end-results.

Of all cases of fibroids and fibrosis uteri which require treatment, I find about 25 per cent are fibrosis uteri cases, for which radium is the safest and most economical treatment, 75 per cent are fibroids, and of these only about one-third are suitable for radiation; the balance must be treated surgically.

In the fibrosis uteri cases my results with radium show practically 100 per cent success, and I feel that it ought to be strongly emphasized that one is hardly justified in treating them otherwise.

A careful study of our best authorities shows an unanimity of opinion that radium therapy has a definite place in the treatment of fibroids, and that the type of case to which it is applicable has become well standardized. We must, however, always insist on the importance of correct differentiation between the indicated and the contraindicated types and that radium be applied only by an experienced gynecologist or a radium specialist in cooperation with him. Frequently the choice of treatments cannot be made until after examination under anesthesia, and the patient's permission should have been obtained by the surgeon to proceed as he thinks best.

It should be an absolute rule that a diagnostic curettage be done in every case of uterine hemorrhage before radiation. In six cases not counted in the present series, carcinoma of the body was discovered by the curettage, one of these in an unmarried woman of twenty-nine. And

it is universally accepted that panhysterectomy is the best treatment for carcinoma of the body of the uterus.

Radium and surgery should not be in competition. We must determine what is best for each case and should be careful not to generalize too much. However, end-results are so satisfactory in those cases where radium may replace surgery that I am convinced that every gynecologist should be equipped with radium of his own, or be able to obtain its use just as he is with the knife or cautery. He should carefully perfect himself in its technic and be as confident in treating a case with radium as he would with surgery.

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THE EFFECTS OF X-RAY AND RADIUM UPON THE FETUS IN UTERO*

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CONCERNING the effects of radiation upon living tissues and embryonic life we have heard much. A vast number of reports of experimental work along these lines is on record. Since it was first suggested that the x-ray might be used in the diagnosis of pregnancy, the possibility of injuring the fetus in utero has been visualized, but the amount of experimental work carried out to demonstrate the truth or falsity of this contention is insignificant in comparison with that produced in connection with other biologic questions brought up by the continually increasing employment of radiation in therapeutics.

It early became known that exposure of the generative system to continued dosage of either x-ray or radium would produce sterility in human beings. This was first observed in practice and then experimentally demonstrated upon animals. Workers with these media then

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took measures to protect themselves as they carried on their activities, and in treating patients the possibility of producing sterility came to be debated regularly as one of the drawbacks to treatment which must of necessity involve the genital organs. Chiefly was this true when women of child-bearing age must undergo treatment for benign uterine tumors. Carcinoma of the uterus seldom occurs in women still young enough to bear children. A few instances of malignancy complicating pregnancy are reported in literature, but it must still be looked upon as an occurrence of comparative rarity. Fibroids of the uterus, on the other hand, are exceedingly common in women still in the child-bearing period of life. When a woman has attained menopausal age, cessation of menstruation and enlargement of the uterus may indicate either tumor growth or pregnancy. Differential diagnosis is by no means easy even when no untoward symptoms are present. When pathologic conditions are in evidence, which may or may not be the result of tumor growth or pregnancy, the diagnostician's perplexities are greatly increased. The continually extending employment of the x-ray for the diagnosis of pregnancy, and of radium and x-ray for the treatment of fibroids, introduces a still further element of confusion, as well as adding a very real danger to a condition which at best is hazardous alike to the patient's life and the physician's diagnostic reputation.

The possibility, as well as the wisdom of voluntarily producing sterility in women still capable of having offspring, has as a result been very much debated. We have had a multiude of reports concerning women subjected to radiation for one reason or another who have later become pregnant, with detailed examinations of the condition presented by the resulting progeny—mental, physical and spiritual. We have experimented and reasoned all the way from Mrs. Common- or House-Mouse to the married graduates of our leading coeducational universities, and the evidence deduced is so contradictory and confusing that we know but little more than when the inquiry began.

When I first set out to collect data concerning the possibility of injury to the fetus *in utero* by exposure of the mother to radiation, a long list of references was quickly gathered. But when the material thus made available was carefully examined, I found that the part actually related to my subject was almost negligible and that this particular phase of a decidedly extensive inquiry has hardly been touched upon. Moreover, no definite distinction is made by the majority of writers between the effect which radiation might have upon progeny conceived and matured by a mother subjected to radiation, and the effect which radiation applied directly to the fetus after conception and partial maturity had taken place might have upon that fetus. Yet this distinction seems to me perfectly clear, and, moreover, so highly important that in the end I had to reject the great bulk of the data collected as not pertinent to the subject in which I

was interested. My concern is with the fetus primarily, with the mother and the maternal organs only secondarily. This differentiation was insisted upon by Driessen, who wrote of the effect upon the maternal organs, particularly the damage that might be suffered by the follicle or the ovum previous to fertilization. Some of his experiments, however, had to do with the effect upon the fetus in utero, and I shall therefore refer to them again a little later.

Let us first consider what the results of animal experimentation have contributed toward elucidation of the question before us. Several authors have already tabulated this, so I shall take the liberty of making use of their conclusions.

Bailey and Bagg, writing in 1923, reported the results of their own experiments with irradiation with radium and added a number of instances where the condition of the fetus subjected to x-ray radiation while in the uterus had been studied postpartum. They aver positively that "the results of experimental studies in this field are conclusive in agreement that detrimental disturbances occur in animals that are exposed to a sufficient amount of irradiation during the various stages of development. This is probably due to an arrest in the orderly sequence of embryonic processes, and the type of resulting monster is apparently determined by the developmental period at which the exposure is given."

Pregnant rats when exposed to radium irradiation near the end of the gestation period afterward gave birth to young which either died shortly after birth, or showed deformities. The surviving young had brains with practically no cerebral cortex, their eyes were sightless, and they later proved sterile in both sexes. The intravenous injection of an active deposit of radium emanation was also used by Bagg in his experiments, the usual dose being about five millicuries of radium emanation. These injections invariably produced either death and absorption of the fetus or abortion, depending upon whether the radioactive substances were used early or late in the gestation period. Subcutaneous areas of extravasation which characterized some of the surviving young were found to be peculiar to the offspring of the irradiated females alone. Working in conjunction with Little, Bagg obtained similar results by applying x-rays to pregnant mice, they being able to produce deformities of the legs, feet, head and eyes. Hansen had results similar to Bagg's with radium, when he employed the x-ray upon pregnant rats. Hippel and Pagenstecher treated pregnant dogs with x-rays, obtaining live puppies with cataracts from some litters, but more often fetal death and abortion. The French experimenters, Regaud, Nogier and Lacassagne, caused abortion in dogs by application of x-ray, while from Germany, Cohn, Lengfellner, Krukenberg and Walter likewise reported that the exposure of dogs in whelp to x-ray resulted in the production of deformities of the progeny in utero.

Most of the observations just noted were made a number of years ago, those of Bagg and Hansen being the most recent. The entire subject was reviewed by de Nobele and Lams and presented with an account of their own experiments before the International Radiological Congress which met in London in 1925. They made use of guinea pigs and rats as experimental animals, as Lams has given especial attention to the sexual physiology of the guinea pig, and the same has been done for the rat by the American investigators Long and Evans and the Japanese Ishii. Of the rabbit, the experimental animal most used in France, far less is known, and the transfer of experimental results from animals to human beings is therefore much more difficult. Though they employed x-ray, it is their belief that exposure to radium rays of similar wave length would bring about practically

identical results. In general, the more penetrating the ray, the more pronounced were the results obtained. If irradiation took place soon after conception, the embryo was immediately killed. Later irradiation did not always result in the death of the embryo, though abortion was the most common outcome. Those embryos which survived were abnormal, usually frank monsters. Irradiation late in gestation, when the embryo was near complete development, almost always induced abortion; these results duplicate those obtained by Schinz who worked with rabbits.

In a series of animal experiments to which reference has already been made, Driessen found that rabbit embryos underwent undoubted transformation when the pregnant female was exposed to irradiation. The duration of gestation was prolonged and the resulting offspring, if they survived at all, were distinctly abnormal. By exposing only one side of the animal to the rays, this investigator was able to kill the embryos in the uterine horn of that side, though histologic examination of the uterus itself demonstrated no noticeable changes in the structure of that organ or in the corpora lutea. It is Driessen's opinion that a brief exposure, such as might be employed for diagnostic purposes, would not necessarily injure the fetus in utero, but that caution is necessary not to make exposure unduly long, nor to repeat it, should the first attempt prove unsatisfactory, as repeated exposures apparently produce a cumulative effect which is especially dangerous.

The latest record of animal experimentation along these lines appears to be that of A. S. Parks, reported to the Royal Society last year. His observations were made in the course of an investigation of the causes and physiologic phenomena of menstruation. Irradiation of the female genitalia in both gravid and nongravid animals was one of the features of this study. "The most striking result of the irradiations during early pregnancy" he found to be "that in almost all animals irradiation caused the pregnancy to terminate. The usual course of events was for the estrus to reappear soon after irradiation. . . . These results clearly indicate that the persistent corpus luteum of pregnancy is caused to undergo premature retrogression by exposure of the animals to x-rays. This, however, does not necessarily mean any direct effect of x-radiation upon the organ. The most probable hypothesis is that the fetuses were adversely affected by irradiation, and that their death was followed in the ordinary way by the involution of the corpora lutea."

Nowhere have I found any records of animal experiments where pregnant animals were exposed to radiation without any effect, immediate or remote, upon mother and offspring. This may be simply because no one has been sufficiently interested in combating the prevalent impression that irradiation of the gravid uterus is fraught with grave danger to its content, to collect observations to the contrary. It may also be because no such observations have ever been made. Certainly the general impression gained from perusing the literature of animal experimentation is that injury to the embryo is practically certain to occur.

Turning now to the effects upon the human embryo, we find a rather wider range of observation and, in the case of those who desire to employ the roentgen ray for the diagnosis of pregnancy, a distinct motive for proving that radiation of the pregnant uterus is a safe procedure both for mother and child.

In 1924 we find Reuben Peterson complaining that gynecologists and obstetricians had not promoted the roentgenologic diagnosis of pregnancy because they

"feared to use it in pregnant women on account of its effect upon the fetus." He then assures us that the last question has been answered practically by the results of thousands of diagnostic exposures where no appreciable harm resulted in either mother or fetus, and he goes on to say that it must be borne in mind that there is a vast difference between diagnostic and therapeutic roentgen-ray dosages. Hickey, the head of the radiology department in his university, "has figured that the current for ordinary diagnostic roentgen-ray work is not more than a fiftieth as strong as that used for therapeutic purposes where bad results have been reported, so far as the early embryo is concerned, and he had assured the gynecologist "that there is absolutely no danger to the fetus at any stage of gestation provided the exposures are short and not too frequently repeated."

A consideration of the literature lends support to Peterson's position, which I am assuming to be typical of that of the majority of those members of our profession who have interested themselves in this form of diagnosis. Even if a certain percentage of mothers diagnostically exposed to x-rays later gave birth to malformed or mentally defective children we would have no right to assume that the x-ray had anything to do with this until a careful comparison was made between the percentage of anomaly presented by a large series of x-rayed cases with the percentage of anomaly occurring in births in the general population where no x-ray exposures had been made. No one has attempted to compile these figures so far as I am aware, and we must not forget that mental deficiency, hydramnios, clubfoot and similar malformations and monstrosities, existed before Conrad Roentgen himself was born. We are, I think, justified in dismissing from consideration, the injuries possibly sustained by the fetus subjected to diagnostic x-ray within the uterus.

Several comparatively recent articles have surveyed the literature since 1914 relating to injury of the fetus in utero by the therapeutic application of x-ray, and since 1923 radium radiation has also shared in the responsibility for such injury.

Abels canvassed the subject quite thoroughly, as did also Zappert, their reports covering largely the same ground. Zappert collected twenty-one observations where there was likelihood of the fetus having been injured by x-ray or radium treatment of the mother, and less than half the children born under these circumstances, could by any possibility be rated as normal. Most of them were underweight and presented other indications usually associated with prematurity. In a relatively large number of cases microcephaly was present, and some of these babies had microphthalmia as well. This author calls attention to the rather impressive circumstance that the most carefully and scientifically observed cases always showed graver disturbances of development than did those which were more casually observed and recorded. Driessen's reports of observations on human subjects also coincide with the authors just mentioned. In the United States Mundell of Washington, D. C., reported a case of carcinoma in a pregnant woman treated by radium applications, which was promptly followed by abortion. He collected fourteen cases where radium was used during pregnancy with no appreciable effect upon the fetus, but offset this by a list of fifteen where abortion, fetal anomaly and early death were the outcome. Most of his collected cases were included in the lists of the European writers already mentioned.

Examination of the material thus gathered shows a very striking agreement in all the main contentions. Very early irradiation appears to induce abortion quite regularly when x-ray or radium is therapeutically applied. Later applications of radiation would seem to retard the normal development of the fetus and to induce abnormalities, especially of the eyes and brain. The abnormalities reported are substantially the same in the majority of cases. In that of Ries there were anomalies of the genitourinary apparatus in addition to deficiencies in the skeleton, but, as the author points out, our knowledge of fetal development precludes our attributing the occurrence of these to irradiation of the mother which did not take place until one hundred and twenty-one days after the calculated beginning of pregnancy. Moreover, the mother in this instance was herself defective, a cretin, and as the child was illegitimate, no information about its paternity could be obtained, so that the inference is very strong that radiation was only in small part responsible for the fetal malformations in this case.

A much better illustration is the case of Naujoks, whose patient had given birth to a normal child before she developed sarcoma of the ovary. Following operative removal of this growth she received prophylactic roentgen irradiation and became pregnant either during or soon after this treatment. The second child was apparently born at term but from the first did not appear normal. At one year there was microcephalus and indications of deficient mentality. The mother remained well and bore a third child which was healthy and apparently normal at three months of age. The second child at two years of age, on the contrary, was extremely small and weak, with a head like that of a bird. She was of very irritable temper and had not begun to talk. The author believed her to be idiotic. The difference between the child irradiated in utero and the two others of the same parentage and environment who had not was very striking. Abel's patient had previously had three children. She was irradiated during what proved to be the third month of pregnancy. The author emphasizes the fact that the child was born at full term, as it had fully developed nails, the testicles were descended and lanugo was present. The head, however, was typically microcephalic, and there was also double microcornea and microphthalmus. The penis was less than 5 mm. in length and had no corpus cavernosum. The muscles of the lower extremities were slightly spastic. X-ray examination of the long bones showed alterations which were suggestive of syphilis, but the Wassermann reaction was negative, and there was no history nor other stigmata which would have confirmed this suspicion. None of the mother's previous children had displayed similar manifestations. It is only fair to recognize, however, that the neoplastic disease for which the mother was treated by radiation may not have existed at the time of the previous pregnancies.

According to Bailey and Bagg it is the severity of the treatment, as well as the period of fetal development during which irradiation took place, which determines the particular reaction of the individual fetal tissues. One of their patients had local treatment of the vulva during the fifth month of gestation, which they evidently looked upon as light. At the eighth month the mother was treated over the vulva with gamma-ray radiation, equivalent to 50 per cent of the erythema skin dose. "The treatment was not severe, the fetus was not directly irradiated, the child was apparently normal at birth and has remained so up to the present time." Judging from the clinical reports they have studied, these authors have formed the opinion that in those instances where comparatively great disturbances have resulted in the child, the irradiation was given early in pregnancy. Driessen expresses similar sentiments, the younger the embryo, the greater the injury. While he willingly makes allowance for the possibility that some of the abnormalities appearing were not in any way due to the effects of the roentgen rays, the evidence that the rays

from radium and x-ray do injure growing tissues, including those of the embryo, is too overwhelming to be ignored. Mundell admits that though it may very well be argued that the deformities of the babies born of mothers who had undergone treatment for malignancy or fibroids might be due to the maternal weakness, "the reporters in each instance were of the opinion that the deformity was the result of radiotherapy. Also such malformations have not been noted heretofore in children born of mothers who were suffering with cancer of the cervix, before the advent of radium therapy. Therefore, it would seem safe to say that such conditions are not merely coincidences."

It is my personal belief that the evidence so far collected is overwhelming in its demonstration of the dangers of using x-ray or radium upon a pregnant woman when there is reason to hope the pregnancy can be continued to full term. Every gynecologist should make certain that pregnancy is ruled out before he begins treatment for either benign or malignant conditions of the female generative apparatus. In the rare coincidence of pregnancy and cancer of the cervix, the usual considerations governing the production of abortion will have to be marshalled and debated. In a personal communication from Joseph Muir of New York, he stated emphatically that radium dosage sufficiently high to be effective in controlling cervical cancer would undoubtedly be fatal to the fetus in utero. He added that inasmuch as it is unreasonable to expect a woman suffering from such a malignant disease to be able to carry to term and deliver a normal healthy child, he felt that there was no question of the advisability of immediately emptying the uterus. I am fully in accord with him in this. The question here is not whether the life of the fetus should be sacrificed, but whether therapeutic abortion is, under the circumstances, the course which should be pursued as offering the greatest chance of saving the life of the mother.

As the situation just cited is fortunately rare, the irradiation of women suffering from uterine fibroids or similar benign conditions presents a problem much more likely to be offered to the gynecologist. Confusion between the fibroid and the pregnant uterus has occurred often in the past, and even with the greatest diagnostic care, is almost certain to take place in the future. Again, fibroids and pregnancy may exist together. If a pregnant woman is thus inadvertantly radiated, what is the proper course to follow? Should the pregnancy be allowed to continue to term if it will, or should the strong probability of the product of gestation being deformed or otherwise abnormal constitute an indication for its interruption? Some of those who are enthusiastic advocates of the diagnostic use of the x-ray may come forward at this point and suggest that during the later months of such a pregnancy it will be possible to determine by the fluoroscope whether or not the fetus in utero is microcephalic or otherwise malformed. This is, of course, quite possible, but I cannot feel that our problem could be solved so easily. Due care in the selection

of cases subjected to x-ray or radium treatment is our greatest safeguard. Even in elderly women the history should be minutely scrutinized, and the possibility of pregnancy should be kept continually in mind. Only in this way can the gynecologist and radiologist obviate much human suffering and at the same time avoid personal chagrin.

CONCLUSIONS

1. Diagnostic exposure is not harmful unless resorted to too frequently.

2. Therapeutic exposure causes abortion in the early months and various deformities of eyes, brain and cord during the later months.

3. The severity of dosage and the period of fetal development determine the particular reaction of the individual fetal tissues, the younger the embryo the greater the injury.

4. Malignancy superimposed upon pregnancy demands measures sufficient to destroy cancer, the life of the fetus, of course, being disregarded.

5. In obscure cases, pregnancy and fibroids coexisting, and in elderly women, the probability of pregnancy should always be kept in mind in order to avoid subjecting the supposedly absent fetus to immediate death or to something worse.

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RADIOTHERAPY IN THE TREATMENT OF CANCER OF THE CERVIX*

With Comments on Modern Variations in Its Application

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RADIUM therapy is so well established in North America as the most valuable single therapeutic agent in the treatment of cancer of the cervix that any further statistics or supporting arguments in its favor would be superfluous. My participation in this discussion will therefore be restricted to a few comments on the general practices of the profession, the various ways in which irradiation is utilized, the necessity for accurate diagnosis, the importance of recognizing the contraindications for radiotherapy, and the hazards involved in its use by the inexperienced.

In visiting different clinics, I have been impressed by the diverse designs of radium applicators and the variations in technic. Some operators use one of the salts of radium, others the emanations only. Massive doses are insisted upon in several institutions, while divided doses are believed to be equally efficient in others. Probably most of these differences are relatively unimportant, provided an ample amount of radium is available, the screenage is correct, and all properly selected cases receive full dosage. I must confess, however, that the forcible and wide preliminary dilatation of the cervix with a branched dilator, before the introduction of a bulky applicator, that I observed in one large clinic was a distinct shock. One could almost visualize this squashing trauma disseminating malignant cells throughout the pelvis. I believe that it is highly desirable to use as small and slender an intracervical applicator as possible.

The homogeneous localized cross-firing resulting from intratumoral transfixation with gold or platinum seeds or platinum-iridium needles, inserted in the lesion at equidistant points, constitutes a definite step in advance in cervical cancer therapy. Personally, I have been using transfixation needles in conjunction with intrauterine applications for the past seven years, with markedly better results.

Despite the encouraging statistics from the Radium Institutes in London, Paris, and Stockholm, many Continental gynecologists are still enthusiastic advocates of radical abdominal hysterectomy. Weibel in Vienna, Warnekros in Dresden, Faure in Paris, and Bonney in London have done a tremendous number of these operations, and each

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one claims a primary mortality of less than 8 per cent, with a very satisfactory number of five-year cures. It must be remembered, however, that these men have developed their technic over a period of years, are unusually skillful pelvic surgeons, and probably have had to adapt their needs to their circumstances following the Great War; and most of them admit the value of postoperative radiation. Toth of Budapest is an ardent protagonist of the Schauta vaginal hysterectomy, but he urges the use of postoperative radiation to control the remote lymphatic chains, inaccessible during the course of the operation.

While radical abdominal hysterectomy is thus a competitor of radium treatment, at the present time roentgen-ray therapy is used chiefly to supplement the primary operations or radium applications. That it has a distinct field of usefulness in destroying metastases in the perimetritic structures, no one can deny, but most roentgen-ray therapists now concede the superiority of radium in the attack on the cervical lesion. The technic described by Schmitz,[1] whereby the entire pelvis is cross-fired with x-ray with almost mathematical exactness, is to be strongly recommended.

Preoperative radiation has lost its early prestige, probably because so few radical hysterectomies are done in this country. Some years ago I favored combined radium therapy and operation above all other methods of treatment, and continue to take advantage of it occasionally. In one patient, only thirty-two years old, with a moderately advanced squamous cell cancer, in whom a radium dosage of 4320 mg. hr. had apparently eventuated in complete macroscopic disappearance of the tumor and normal uterine mobility, the extirpated specimen showed a nest of cancer cells 5 mm. in diameter, surrounded by connective tissue and considerable leucocytic and lymphocytic infiltration. This patient was operated upon nearly five years ago, and is still alive, well, and free from evidence of recurrence. I believe that postradiation hysterectomy has a place in the treatment of comparatively young women, whose biopsy specimens show ripe tumors with hornification. If the operation is deferred until at least three weeks after the last radium application, hemorrhage will have ceased, there will have been an opportunity to reinforce the patient's vital resistance, and the hysterectomy need not be so extensive as the classical Wertheim operation. Following this course of procedure, the primary operative mortality is negligible. In general, however, I am in accord with the majority that with few exceptions most cases of cancer of the cervix are best treated with radium, followed by x-ray. At the New York Post-Graduate Hospital, I give all but hopeless patients 4000 to 5500 mg. hr. of radium therapy in divided doses. Immediately thereafter, these patients are referred to the Department of Roentgenology, for high voltage deep x-ray therapy. The director of this depart-

ment calculates the appropriate dose for each patient, and usually makes an application on four successive days, using the lower abdomen twice, the sacral region once, and the perineal region once, as portals of entry. The sole indication for reduction of dosage in irradiation that I have observed has been an abnormal retention of nitrogenous waste products in the blood, or other evidence of markedly impaired metabolism.

Combinations of radium therapy with cauterization, electrocoagulation, etc., are still in the experimental stage, but I think that most of us, having an adequate quantity of radium, regard the advantages of such methods as at least questionable.

The aphorism that intelligent treatment is predicated upon accurate diagnosis is almost bromidic. Yet, a patient with a lesion simulating cervical cancer presented herself four years ago, who had been treated with radium for two years by a specialist in radiotherapy. The reports on repeated biopsy specimens described endocervicitis only, but the physical appearance of the cervix, together with the persistence of spotty bleeding at intervals were evidently regarded as sufficient justification to disregard the laboratory reports. Pathologic examination of the specimen that I removed by panhysterectomy showed the endometrium and tubal mucosa to be a mass of tuberculosis. In another instance, a bride, twenty-five years old, consulted me after one radium treatment at another hospital for "cancer of the cervix," without improvement in the appearance of the local lesion. The Wassermann and Kahn tests were strongly positive and antisyphilitic treatment effected a prompt cure. It should never be forgotten that tuberculous and luetic lesions of the cervix closely resemble carcinoma at times, and suspicion should be aroused in every case in which the biopsy report fails to corroborate the clinical diagnosis. I presume that the desirability and safety of biopsy specimens require no defense before this Association.

The recent enlightening publication of Healy and Cutler,[2] demonstrating conclusively the pronounced radiosensitiveness of unripe cancers of the cervix, notwithstanding their greater malignant potentialities, as compared with the slowly invading but more highly resistant ripe tumors, explains the sometimes unexpected satisfactory results from radiation in apparently advanced cases.

Although radiotherapy is commonly regarded as unattended by mortality, one of my colleagues and I have each had one patient who died from acute peritonitis, due to a failure to recognize a latent salpingitis at the time of the radium application. I had a second patient who also developed peritonitis but recovered. One cannot be too careful in excluding purulent accumulations in the pelvis before applying radium or x-ray. If their presence is discovered or even suspected, it is prudent to operate first. The hopelessly advanced cancer in the

patient approaching her end is also a contraindication for intensive irradiation, although a moderate dose of radium will often serve to arrest bleeding and control the malodorous discharge.

A protest should be registered against the indiscriminate and unrestricted distribution of active applicators by commercial organizations to all physicians who are willing to experiment with radium therapy on patients who are capable of paying the fees demanded by these companies. I have seen several patients who have been deprived of whatever chance of cure they once had, or whose bladder or rectum have been irreparably damaged, by underdosage, faulty application, or improper filtration. No one should essay the treatment of a patient with cancer of the cervix unless he has at least 125 mg. of radium, properly screened, in applicators adapted to the cervix and uterine cavity, with a mental picture of the pelvic pathology, a knowledge of the physics of radium, a clear conception of the histopathologic changes which follow irradiation, and a certain amount of experience.

Finally, I would venture the assertion that the details of the treatment of each individual case of cervical carcinoma should be directed by a physician who is a competent pelvic surgeon and who has both an adequate supply of radium and ample roentgen-ray facilities at his command. Only under such circumstances will his advice be unbiased.

CONCLUSIONS

1. Radium is the most efficient single therapeutic agent in the treatment of cancer of the cervix.

2. Variations in technic are relatively unimportant, provided an ample amount of radium is used, screenage is correct, and sufficient dosage is given.

3. Slender intrauterine applicators and intratumoral transfixion with needles are conducive to good results.

4. The sustained popularity of radical hysterectomy abroad is probably due to the concentration of radium in a few institutions.

5. Combined radium therapy and operative treatment is of value in occasional selected cases.

6. Roentgen-ray therapy should be used chiefly to supplement a primary operation or treatment with radium.

7. The appearance of some tuberculous and luetic lesions of the cervix simulates carcinoma.

8. Patients with metabolic impairment, pelvic suppuration, or hopelessly advanced cancer are not candidates for intensive radiation.

9. The indiscriminate distribution of radium apparatus to the profession in general is to be deplored.

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PYOMETRA FOLLOWING RADIUM THERAPY FOR UTERINE CANCER*

By P. Brooke Bland, M.D., Philadelphia, Pa.

CERVICAL atresia with retention of infected material within the uterine cavity, customarily called pyometra, has generally been regarded as an entity of rather infrequent occurrence. Compared with other lesions of the uterus it may still be included in the category of rare conditions, although I believe the incidence of the malady has expanded considerably during the past decade. Since the advent of radium as the preferential recourse in the treatment of cervical carcinoma, pyometra is being encountered with increasing frequency. Prior to the adoption of gynecologic radiology, the disorder was rarely seen, even by the pelvic surgeon of wide experience. This is in sharp contrast with the experience of those in active work today, for in a large number of communications received from my contemporaries in all parts of the country, all except one report cases arising in their practice, ranging from one to ten.

This material was gathered, I might add, in spite of the fact that my letters of inquiry received the rather characteristic indifference usually accorded the questionnaire.

The information submitted, however, indicates that pyometra may be looked upon as a comparatively new entity, at least from the standpoint of the clinician, because it is altogether likely that the large proportion of cases observed arose during the last ten and probably for the most during the last five years.

Even with the increase in the number of cases encountered, this form of pyometra, according to Lammers, of the Radiotherapeutic Institute of Rotterdam, seems as yet generally unknown. Since the complication is gradually becoming more prevalent, perhaps it should not be placed in a nomenclature relating to it alone. I can readily perceive that it probably would be objectional, if not unscientific, to apply the term radium or postirradiation pyometra, though it is clear today that of the numerous etiologic factors, radium is the most conspicuous.

I recall two cases only that can be attributed to causes other than the element named. One resulted from carcinoma of the cervix, the most common cause of pyometra prior to the employment of radium therapy, and the other occurred, as nearly all noncancerous cases do, in an elderly woman with senile fibrosis of the cervix.

It may be of interest to mention that in nearly all countries except

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America, the condition, owing to its increasing frequency, has aroused considerable clinical interest. Here the etiologic relationship of gynecologic radiology to pyometra seemingly has not been recognized or appreciated, for in a careful perusal of the current literature of America, I was unable to find a single reference to the trouble. The British, Dutch, Swedish and especially the French literature contains numerous case reports and rather lengthy articles dealing with the subject. The condition has, however, aroused more interest in France than elsewhere and, hence, most of the articles describing postirradiation pyometra are found in the French publications.

Even with these references the malady has not been accorded the attention it deserves. That the entity thus far has received only the most meager publicity is probably accountable for the fact that it is more or less new, not suspected and, hence, not generally recognized.

ETIOLOGY

At the outset one must insist on the term pyometra and not establish confusion with uterine cancer accompanied by more or less purulent discharge. The characteristic of pyometra is distention of the uterus with pus. This is the analogy in the uterus of pyonephrosis in the kidney, where the dominant character is not the suppuration but retention with distention of the organ.

It is, of course, obvious that the accumulation within and distention of the uterine cavity with suppurative material may result from any condition producing a partial or complete obstruction of the cervical canal. The causes, therefore, may be manifold. Cases are recorded as resulting from inflammatory edema about the internal os and senile fibrosis of the cervix, as occurs in women advanced in years, is sometimes influential. Endometrial vegetations or polyps springing from the region of the isthmus and occluding the internal orifice of the cervical canal are mentioned as causative as well as malpositions of the uterine body.

Benign neoplasms, in the form of myomas plugging the cervix, have been accountable and cases have resulted from chemical ulceration followed by fibrosis.

Congenital gynatresia may be responsible, but a lesion of this type is almost invariably associated with hemato- and not pyometra.

Heretofore occlusion from carcinoma of the cervix has been designated as the most common cause.

Statistics regarding pyometra, however, as a complication of cervical cancer are far from uniform, ranging from 3 to over 10 per cent. Alamanni, from a study of his personal cases, believes that 3.3 per cent of cervical cancers are associated with stenosis of the cervix, with pyometra as a sequel. Lomon quotes figures of a like percentage. Sainclair sets the percentage as high as 6.2 and Tate as high as 10.7

per cent. These figures are somewhat antiquated, and I believe were drawn from conclusions founded on data more or less in error, probably from regarding cases of advanced cervical carcinoma with malodorous discharge as pyometras.

From a fairly large experience with uterine cancer, extending over a period of several years, I feel reasonably certain that the percentages quoted, especially the higher figures, by the authors named, are far too high.

Personally I do not believe that pyometra complicating cancer of the cervix goes beyond, if it really reaches, one-half of one per cent.

Radium as the accepted mode of treatment of cervical carcinoma has materially increased the incidence of the complication, though to what extent, owing to the scant information now available, is impossible to say.

From a study of my personal cases of cervical cancer treated with radium, I found that approximately one out of every 100 developed pyometra. It is not unlikely that the study of a large series of cases will disclose figures somewhat in excess of one per cent for the complete and considerably more, probably 3 to 5 per cent, for the incomplete type.

Norris, in 600 cases of carcinoma of the cervix exposed to radiotherapy, reports 5 cases of pyometra. Kelly has treated more than 1900 uterine cancers with radium and has observed several cases of pyometra subsequently, though the exact number is not known. Polak reports 7 cases of pyometra following irradiation of the cancerous cervix.

It will not be possible, however, to even estimate roughly the incidence of postirradiation pyometra until an opportunity is afforded to systematically study a large series of cases, or in other words, until the gynecologic radiologist uniformly reports his observations regarding the complication.

I am persuaded that the malady, especially the incomplete variety, is much more frequent than hitherto suspected. The frequent complaint of patients suffering with odorous discharge extending over a period of several weeks or months after the application of radium, has led me to speculate as to whether partial stenosis of the cervix is not responsible in a certain number of cases.

Is it not possible that some of these patients are victims of partial cervical stenosis with intermittent pyometra? These cases are by no means rare and I am inclined to believe that partial occlusion of the cervix with retention of infected material within the uterine cavity is the factor chiefly responsible for the symptom.

TYPES

From what has already been said regarding discharge and other features of the trouble, it is discerned that cervical atresia is sometimes

incomplete. With the canal occluded completely, it is obvious that all of the infected material would be imprisoned within the uterine cavity. One may legitimately divide, therefore, postirradiation pyometra into two types, (a) incomplete, and (b) complete.

At the outset I am quite confident in stating that the incomplete form is by far the most frequent, though the second variety is by no means rare.

In the partial type the chief symptom, as I shall mention later, is a purulent, offensive discharge. Occasionally it contains blood, though this is not, as in cancer, present invariably. Lomon and others state that in the large proportion of cases it is entirely absent. In the second or complete form all the infected material is retained within the uterus and the principal symptoms are at first wholly subjective.

ORIGIN

With respect to the mode of origin or development of postirradiation pyometra, it is necessary to recall the effect of radium on neoplastic tissue in general, converting it into dense fibrous material.

The typical picture of the cartilaginous or frozen cervix, postirradiated cancerous cervix, needs no discussion. The formation is due fundamentally to fibrosis, followed by contraction and cohesion or fusion of the cervical walls.

The fluid accumulation results from associated inflammatory changes in the endo- and myometrium, lesions almost invariable accompaniments of cervical carcinoma. That the fluid is inflammatory in origin is based on the observation that the normal secretion of the endometrium is almost nil. According to Lomon, it is insufficient to create, even in cases of atresia of the cervix, an appreciable collection.

With respect to infection, one may say that a cancerous area is literally blistering with all forms of pathogenic bacteria and, hence, the accumulating fluid becomes infected from a cavity already teeming with infectious organisms.

ONSET

The onset of the condition and its progress of development are variable. With the influence of radium on tissue reaching its acme in the course of from four to six weeks, it would seem that in an additional number of weeks or approximately three months, fibrosis would be more or less complete. Following this stage contraction must inevitably ensue, but the phenomena that determine why in some instances the fibrosis terminates in stenosis, incomplete or complete, are not understood.

In a small number of cases the pyometra, owing probably to a cervical canal already partially barricaded with carcinoma, develops within a few weeks after the application of radium.

Gellhorn refers to a case of inoperable carcinoma of the cervix which he "needled." Three weeks after the application an acute pyometra developed. This increased with extraordinary rapidity and extended nearly to the umbilicus. He attempted to open and drain the uterine cavity through the cervix, but was prevented by the densely organized mass of scar tissue.

It might be interesting as well as profitable to mention parenthetically that this patient, though intensely ill, was given milk hypodermically and after twelve injections the uterus was practically of normal size. Gellhorn reports a similar experience with another patient.

However, rapid development is not the rule and I believe that more than 75 per cent of the cases are of a semichronic type, developing slowly and not giving rise to symptoms before three or six months. Polak's cases arose within three and all of Norris's within six months. Spalding observed one case in a patient four weeks after irradiation and in another seven months following treatment. Sireday and Gagey, in discussing this feature of the trouble, report one case of pyometra arising two years after the application of radium.

In a small number of instances the process of development is extremely tardy and symptoms may not arise for a year or more. In three personal cases subjective symptoms, expressed in pelvic discomfort finally amounting to severe pain together with tenderness and uterine enlargement, arose in two patients at the end of two years and in the third at the end of seven years. In the first two patients the symptoms at the beginning were not severe, and they did not apply for relief until three years elapsed from the date of treatment. The third patient did not consult me until one year after her symptoms began or nearly eight years after the application of radium.

SYMPTOMS

In considering the symptomatology of postirradiation pyometra it becomes necessary, first, to describe the clinical phenomena associated with the partial or incomplete type and, second, those accompanying the closed or complete variety. The former is subjectively manifested by periodic attacks of mild pelvic pain, due to efforts of the uterus to expel the retained material, and an offensive purulent discharge. At times the discharge is tinted with blood, *though this is not constant, differing in that respect from the discharge accompanying uterine carcinoma.* After the expulsion of the collection, mechanically comparable to a miniature labor, the pain temporarily subsides.

In the closed type of pyometra the predominant subjective symptom is hypogastric pain, though this may not become manifest until the pyometra attains considerable dimensions. In the acutely septic cases the symptoms are correspondingly acute, evincing systemically phenomena of a septicemic process, combined with those localized in the pelvis and already enumerated.

With reference to the pelvic distress one may say that pyometrial pain occasionally is extremely severe, sometimes radiating to the loins, the entire abdomen and even to the back.

It should be remembered that the distress ceases after spontaneous evacuation of the accumulated material, to reappear at regular or irregular intervals with the reformation of the pyometra. It seems that the pathogenesis of the pain is quite comparable to colic or "uterine tenesmus" which sometimes, according to Doleris, accompanies "chronic inflammation of the uterus with insufficient drainage." It is important to distinguish the discomfort associated with pyometra from that provoked by cancer itself. This should not be difficult if one recollects the periodic or labor-like phase of the pain provoked by pyometra.

DIAGNOSIS

With regard to diagnosis it may be said that the clinical history alone should lead one to suspect pyometra in patients previously exposed to cervical irradiation who subsequently complain of a purulent discharge, *a discharge not constantly blood tinted*, especially if associated with intermittent attacks of mid-pelvic pain. The expulsion of a large quantity of suppurative material followed by temporary cessation of pain is a symptom of the utmost diagnostic significance. Diminution of the discharge followed by recurrence of the pain, in other words a symptom complex signalizing a reaccumulation, is still more important.

Exploration of the interior of the uterus with a dilator discloses the cavity increased in depth. This procedure usually is associated with or followed by the escape of purulent fluid and temporary alleviation of the discomfort.

In the concealed or complete variety one should seriously think of postirradiation pyometra in patients treated with radium months or years previously who complain of hypogastric distress of increasing intensity, finally culminating in intolerable pain.

With the highly suggestive clinical history and the subjective symptoms named, confirmation is found, first, in a renitent or semielastic tumor projecting above the symphysis and, second, by finding, on vaginal examination, a withered fibroid cervix with an impermeable canal.

The size of the uterine distention is variable, depending on the duration of the obstruction. In two cases I observed, the enlargement corresponded to a three months' gestation and in another case, one of eight years standing, the fundus was slightly below the umbilicus or about the area reached at the fifth month of pregnancy.

With the rather characteristic clinical history portrayed by radium pyometra one should be able to establish a diagnosis with comparative facility, though from a study of the case records thus far published,

as well as from my personal experience with the trouble, I am inclined to believe that only in a small proportion of cases is a preoperative diagnosis made.

In some instances the tumor prior to operation has been looked upon as a myoma and in others as an ovarian cystoma. Only after exposure of the distention through an abdominal incision has the actual nature of the enlargement been recognized.

In one of my cases, owing to the globular contour and semifluctuant state of the tumor combined with an abrupt onset of the pain, I made the erroneous diagnosis of an ovarian cyst with a twisted pedicle. Not until I freely exposed the enlargement through a mid-line incision was the true nature of the condition disclosed. In another case of the complete type a provisional diagnosis of a uterine myoma was made. Disregard of the rather characteristic signs associated with the condition, namely, (a) rapid development covering a period of two years, (b) absence of discharge, (c) inordinate pain, (d) withered impermeable cervix, all diagnostic signs arising in a patient beyond the menopause, led to the error. To recall this rather typical diagnostic silhouette should direct one in paths leading to a correct diagnosis in most cases.

PROGNOSIS

In considering the prognosis one may say that, provided the cancerous state of the cervix is completely eradicated, the ultimate outcome is favorable. In the incomplete type catheterization of the uterus with or without lavage usually relieves the condition. In the complete type, if catheterization is impossible, hysterectomy is indicated. Early recognition of the disorder is of considerable prognostic value, because failure to establish a diagnosis promptly may lead to danger in two respects:

First, by assuming recurrence of the cervical carcinoma, there is danger that the surgeon will make the mistake of administering a new series of radium treatments, a measure which would certainly lead to still more serious consequences.

The second danger lies in the possibility of prolonging the period of complacency or watchful waiting until the retained fluid under high pressure spontaneously rends asunder the uterine wall. This is entirely within the realm of possibility, woefully confirmed in a patient observed in my practice.

This patient was given a 1000 mg. hr. dose of radium for chronic metropathy with menorrhagia. Subsequently she developed a purulent discharge of a gangrenous type. Ultimately this subsided, but cessation was followed by increasing pelvic pain. Three months later I saw this patient in consultation with the family physician and found her suffering with generalized peritonitis.

Twenty-four hours before she was suddenly seized with violent pelvic pain followed by symptoms of widespread peritoneal infection. She was admitted to

the hospital in a most perilous condition and succumbed before any measure could be instituted with the hope of affording relief. Lomon refers to two somewhat similar cases with a fatal termination in each.

TREATMENT

With regard to the treatment of postirradiation pyometra there is not much to say. The subject has already been indirectly referred to in discussing the prognosis.

In all the incomplete cases thus far recorded dilatation or catheterization of the uterine cavity has been sufficient to effect a cure. In other words the establishment of free uterine drainage.

With a cervix absolutely stenotic, the only effective mode of treatment is hysterectomy, a procedure rendered necessary in three of my cases.

The rather characteristic clinical features of postirradiation pyometra are illustrated by the following case reports:

CASE 1.—Mrs. E. J. S., aged fifty-two years. On March 7, 1924, the patient was given a 2400 mg. hr. dose of radium for advanced cervical carcinoma. On April 6, 1927, she again came under observation complaining of severe pain in the hypogastrium and back. This had been present for a period of three months. The patient was examined bimanually and a diagnosis of a uterine myoma was made.

After opening the abdomen, the uterus was grasped with a Vulsellum. This maneuver was followed by rupture of the organ and the escape of a large quantity of pus. Fortunately the operative field was effectively isolated by a gauze cofferdam and no untoward trouble developed.

CASE 2.—Mrs. W. L., aged fifty-six years. This patient, suffering with a uterine myoma accompanied by menorrhagia, was given a 2400 mg. hr. dose of radium on August 10, 1922. On September 21, 1925, she was admitted to Jefferson Medical College Hospital complaining of vague abdominal pain and a blood tinted purulent discharge.

On bimanual examination the uterus was found uniformly enlarged with the fundus projecting above the symphysis. A diagnosis of a myoma was made and accordingly a hysterectomy was performed. The uterus, on subsequent examination, was found to be a large pyometra. A moderately early endometrial carcinoma was discovered springing from the right fundal wall. This imparted to the discharge the significant blood tinted hue.

CASE 3.—Mrs. F. K. K., aged seventy-four years, was seen by another surgeon in July, 1917. A diagnosis of inoperable carcinoma of the cervix was made. No treatment was advised or instituted at this time.

I saw the patient first on January 28, 1918. She was given two 2400 mg. hr. doses of radium and remained well until May, 1927. On June 22, 1927, she was readmitted to the hospital complaining of pain in the lower abdomen, especially in the right side.

On vaginal examination there was found no evidence of recurrent disease, but abdominally a large semi-elastic tumor with its summit approaching the umbilicus was noted. This was somewhat tender, though moderately movable. A tentative diagnosis of an ovarian cystoma with partial torsion of the pedicle was made.

Accordingly an abdominal operation was advised and performed. On exposing the pelvic contents the precise character of the enlargement was revealed and the pyometrous uterus containing more than a liter of foul fluid was removed.

Finally, may I entertain the hope that this paper, though somewhat diagrammatic and brief, may be the medium of stimulating special interest in the subject on the part of the gynecologic radiologist.

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HYPERTHYROIDISM COMPLICATING PREGNANCY*

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THE control of the function of reproduction is, like that of digestion, practically entirely under the control of the vegetative nervous system. The uterus, tubes and ovaries are all richly supplied by the sympathetic ganglia of the pelvis and will function entirely independently of the central nervous system. These functions are apparently further governed in part by the action of certain hormones or secretions of the ductless glands acting directly or indirectly through stimulation of the sympathetic nervous system.

It is not surprising, therefore, that contemplating the physiologic and pathologic changes that occur during pregnancy in the human body, deviations from the normal nonpregnant state can be found in the various ductless glands as an expression of their response to the abnormal stimulus brought about by the pregnant state. Thus it is seen that the anterior lobe of the hypophysis may be greatly enlarged, even to twice its normal size,[1] due to overgrowth of the chief cells which dominate the eosinophilic and basophilic cells forming about 80 per cent of the total cells. The adrenals[2] are less changed grossly, but there is evidence that the cortical portion is markedly increased in size and that the activity of the medullary portion is also increased. The ovary presents the unusual corpus luteum of pregnancy, and the graafian follicles fail to develop during this period. Other less evident functional changes in the interstitial cells may well be present. In addition there is evidence that the thymus, epiphysis, parathyroids, and Langhan's islands of the pancreas are also functionally altered by the pregnant state.

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The thyroid is one of the most noticeably altered of the endocrines during pregnancy. In a large percentage of cases this enlargement can be appreciated clinically, and in some cases there appears first during pregnancy a true adenomatous growth, with symptoms of a toxic adenoma. The pathologic and clinical picture of a true exophthalmic goiter may supervene.

In reviewing the literature one is struck by the fact that no one man has had a wide experience in this type of obstetric complication, and this is one important reason for bringing the subject before this association so that a free discussion will stimulate interest in the subject and add to our information.

I wish to approach the subject from two points of view, namely, from that of the surgeon and from that of the obstetrician. The material which I have collected lends itself well to this grouping of the cases. My own material which was collected at the Research Hospital, University of Illinois, was under my supervision throughout. The other cases have been furnished by my surgical colleagues, Drs. Percy and Nadeau of the Augustana Hospital and Dr. Seed of the Surgical Department, Research Hospital, of Chicago. The pregnant woman who develops symptoms of thyrotoxicosis either may consult a surgeon primarily, whether or not she knows she is pregnant, or she may be sent to a surgeon for treatment by her obstetrician. In either event the determination of the line of treatment is left to the surgeon. Quite naturally his chief interest is in the goiter and its manifestations. Under the circumstances it is logical that he concentrate attention on the management of the goiter problem and that to a greater or lesser extent he disregard the existence of the pregnancy. On the other hand to the obstetrician the goiter and its symptoms are only one phase of the pregnancy, and the latter assumes the major importance. As a result two lines of treatment have been evolved based on these two views. In a given case of thyrotoxicosis, especially the exophthalmic type of goiter, the surgeon may advise that the patient be treated medically with Lugol's solution at bed rest for a period of one or two weeks until the clinical picture improves and the basal metabolic rate drops. He will then advise partial thyroidectomy or ligation of one or both poles to decrease the thyroid symptoms. If in accomplishing this very important desideratum the patient aborts, he regrets the incident but nevertheless feels that this is the wisest course to pursue. He feels that there may result even under the best of medical management a thyrotoxicosis which in itself will produce abortion and may result in the death of the mother whether or not she is operated.

The medical man and obstetricians on the other hand are apt to proceed as follows: The patient is put to bed and on Lugol's solution ten drops three times a day. The basal metabolic rate is carefully determined, and the progress of the case is watched under this management.

If improvement is continuous, they are prone to advise against operation, at least until the viability of the child, at which time the baby is relatively safe even though the mother's condition be somewhat jeopardized by the increased strain of labor. This they advise even if operation has eventually to be resorted to. It was to gain some first-hand information on the correctness of these views that this work was undertaken.

In addition to this we have sought some information concerning a group of pregnant patients who display many evidences of hyperthyroidism without falling into the class of true toxic goiter. It has been our impression for many years that a large number of pregnant women who show some increased nervous instability, have a slightly enlarged thyroid and a fine tremor, were in reality affected by a mild hyperthyroidism. These signs and symptoms we have been prone to regard as neurosis or simply as part of the changes incident to pregnancy without attempting to determine what those changes were fundamentally based upon.

The clinical manifestations of this altered function of the thyroid gland during pregnancy vary greatly in the individual case and to some extent with the type of pathology presenting in the thyroid gland itself.

Group I.—The mildest symptoms noted have been increased nervousness, slight weakness, tremor, tachycardia, sweating and a slight increase of the basal metabolic rate. These women are not seriously affected by the altered secretion of the gland, but neither can the abnormal symptoms they present be totally disregarded nor put down as in the textbooks simply as signs of pregnancy.

Group II.—A second group shows symptoms of a toxic adenoma. The gland is irregularly enlarged. There may be difficulty with respiration and phonation, marked prostration and weakness may be seen. The gland may feel nodular, and the basal metabolic rate is usually markedly increased. The giving of Lugol's solution may distinctly aggravate the symptoms. Tremor, tachycardia and sweating may be marked.

Group III.—The third group comprises those patients with typical exophthalmic goiter symptoms. These patients have a firm, moderately enlarged gland, and usually the enlargement is diffuse. They have, as a rule, marked tremor and tachycardia. Gastrointestinal symptoms are common, such as nausea, vomiting and diarrhea. Loss of weight may be marked, and the basal metabolic rate may rise to plus 100 or more. Iodine in the form of Lugol's solution is beneficial, at least for a time, and the remission of symptoms following its exhibition is a significant diagnostic point. Occasionally symptoms of exophthalmic goiter appear for the first time during pregnancy. In other cases a mild hyperthyroidism is distinctly aggravated by pregnancy. In still

other individuals a distinct hyperthyroidism is ameliorated by the pregnant state, and a relapse follows the termination of pregnancy.

C. P. Howard[3] quotes Charcot and Dock to the effect that "Symptoms of exophthalmic goiter begin during pregnancy or the puerperium in some cases while others improve during pregnancy and do not afterwards relapse."

Maurice Fabre reports a case which developed exophthalmic goiter in October, 1924. Patient had tremor, exophthalmos and a small goiter. The Goetsch test was positive. She was treated by doses of hematoethyroidin. She became rapidly better and was better for four months when a severe recurrence occurred following the death of her six-year-old son. She again became better using hematoethyroidin. A pregnancy started the next month. All treatment was stopped, and in spite of the fact that he expected a recrudescence during pregnancy he found the patient in excellent condition, no tachycardia or tremor, perfect morale, and she assured him that she felt better than she had for a year. Pregnancy, parturition and puerperium were uneventful. The baby was perfectly normal. She nursed the baby, and since delivery her condition has remained satisfactory.

The intimate relationship between the thyroid and the pelvic organs is stressed by Miles F. Porter[5] who reports a case of hyperemesis cured by thyroidectomy. In certain invertebrates the thyroid is a sexual organ and empties through a duct into the genital tract. The thyroid is relatively larger in women than in men. Women are five times more prone to thyroid disease than are men, according to this writer.

Stowe[6] reports a case which developed an acute exophthalmic goiter secondary to tuberculosis of the pelvic organs; patient died during labor.

Goodell and Conn[7] report a case in which a goiter was produced by pelvic tuberculosis and cured by panhysterectomy.

Mussey[8] and his associates found among five thousand and forty-three women with exophthalmic goiters thirty-two who were pregnant. Some of these stated that pregnancy improved their goiter symptoms, while others said it made them worse. Only two developed exophthalmic goiter symptoms during pregnancy. These were both mistaken at first for hyperemesis cases because of the goiter crisis symptoms. None of the mothers died while at the Mayo Clinic, although one is reported to have died during childbirth after leaving Rochester, probably of causes other than exophthalmic goiter. Two abortions and two premature deliveries at six months with two full-term still births give a total fetal mortality of about twenty per cent. They found that the use of iodine solution reduced the necessity for primary ligation of the arteries.

Ten patients with toxic adenomata became pregnant after the hyperthyroid symptoms developed. All the mothers delivered living babies safely except one who had a dead baby due to dystocia. All but one had some operative treatment. The exception delivered normally spontaneously.

Mussey warns against the indiscriminate use of iodine preparations and thyroid extract in pregnant women who have symptoms of hyperthyroidism and especially if these are associated with clinical manifestations of toxic adenoma.

Davis[9] studied the basal metabolism rate in a series of pregnant women to whom he was giving iodine on the strength of Marine's findings of decreased iodine content of the thyroid during pregnancy. He reports observations on thirty-six cases. In nine cases of normal thyroid and normal symptoms he found a basal metabolic rate of plus 2.9 before delivery and plus 4.5 after delivery. In seven cases of hypertrophied thyroid and no symptoms and normal pregnancy he found a basal rate before delivery of plus 22.1 and within eleven days postpartum a rate of plus 3.1. He noted an average normal or slightly subnormal rate in five cases of pregnancy toxemia. Two cases of toxic adenoma were studied. One improved

and went to spontaneous delivery at term after lobectomy, done at the fourth month of pregnancy. The second was carried through under medical management, delivered a normal baby and had a subtotal thyroidectomy twenty days postpartum. One patient with severe hyperemesis gravidarum and symptoms of thyrotoxicosis responded nicely to iodine therapy.

An analysis of the basal metabolic rates in a series of normally pregnant women and in those showing the clinical manifestations of thyrotoxicosis, has disclosed the fact that the laboratory test has backed up the clinical impression in practically all cases. It was found that in those cases showing severe symptoms of hyperthyroidism the basal metabolic rate was as a rule correspondingly higher than in those showing mild or no clinical evidence of the thyroid overactivity.

In those patients showing toxic symptoms of an exophthalmic goiter type the use of Lugol's solution in ten drop doses three times a day caused a marked improvement, and the same observation has been made by Mussey, Davis, and others. We have also noted an acute intoxication following the giving of small doses of Lugol's solution to patients with adenomatous types of goiter. Those patients falling in Group I, I described above, had no iodine. This was omitted so that the clinical picture and basal metabolic rate would not be altered thereby. In Group III there are three cases who were referred to the clinic as hyperemesis gravidarum cases which were found to have acute exophthalmic goiter with severe gastrointestinal symptoms. Davis[9] and Dr. Carl Harper report a similar case, and it is probable that they are much more common than we are accustomed to suppose.

I wish to report in some detail one of these cases partly because it illustrates the condition just mentioned and partly because it represents the most carefully observed case that we have studied.

The patient entered the obstetric department of the University of Illinois, Sept. 15, 1927. She was a colored primipara, thirty years old, married and a factory worker. From her features and color one would say that she was not of pure Ethiopian stock. Her last regular menstruation was April 13, 1927, but she flowed for three days beginning May 10, 1927. The latter part of June she began to vomit, at first only once a day, later progressively more frequently. She had to stop work July 11 because of weakness. About Aug. 1 she became extremely nervous and developed a marked tremor. For a month before entry she vomited day and night. Food stimulated vomiting, and it was frequently preceded by hiccough. Her family history and past medical and surgical history were essentially negative. Her menses began at eleven, were regular, thirty-day type and lasted five days with the passage of some clots. Physical examination revealed a poorly nourished woman whose present weight of one hundred seven pounds contrasted with her normal weight of one hundred forty-six pounds. Her pulse was 140, respirations 32, and temperature 98.6. Her systolic blood pressure was 108, diastolic 52. The positive points in the physical examination were: Neck showed moderate enlargement of the thyroid which was firm and not nodular, and the pulsations of the vessels of the neck were marked. There was a moderate degree of exophthalmos. Her chest showed decreased expansion, respirations were shallow and rapid, breasts were small and firm. The lungs were negative for rales.

Whispered and spoken voice faint. The heart's action was rapid. The apex impulse was not strong with a slight suggestion of a thrill. There was a systolic murmur which was transmitted to the axilla. The uterus was enlarged to about the size of a six months' pregnancy. Reflexes were slightly exaggerated. Vaginal examination revealed no abnormalities. The patient appeared to be extremely toxic and exhausted and was hardly able to stand. The basal rate two days after admission was plus 49. She was seen in consultation by Dr. Seed of the Surgical Department who advised Lugol's solution ten drops three times a day and was in favor of a thyroidectomy as soon as the crisis symptoms subsided. He feared that improvement, if it occurred, would only be temporary and that operation should be done before a relapse occurred. We pointed out the danger of abortion which he admitted but felt it was slight in comparison to that of another thyroid crisis. The vomiting stopped promptly on bed rest and Lugol's solution, and the basal rate remained above normal though greatly reduced. She continued on Lugol's solution from Sept. 19, until Nov. 4, and after a rest of a few days it was commenced again and was again discontinued on Dec. 19 for five days. It was then continued until her delivery. An x-ray taken of her chest was negative for tuberculosis. A film made on Sept. 16, 1927, showed a single fetus; a similar

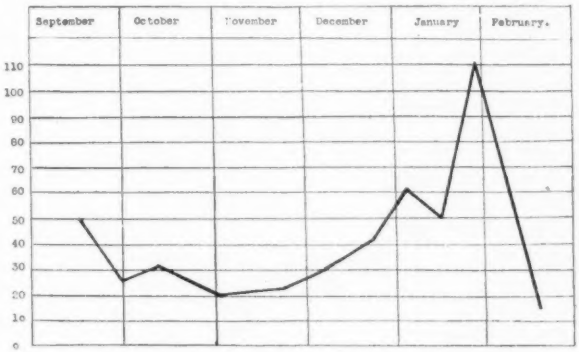

Chart I.

one taken Jan. 3, 1928, showed two babies. Chart I shows the changes of the basal metabolic rate. The red blood count was 4,650,000, leucocytes 13,600. Her general condition was so good on conservative management that we decided to defer operation until some further evidence of thyroid toxemia manifested itself. We found that the basal rate stayed only slightly above normal, that the pregnancy apparently developed normally and that the patient's general condition and nutrition continually improved. She had very little reserve strength, however, as evidenced by her weakness in attempting to get out of bed on several occasions. The iodine solution was stopped twice for a period of a few days, and this was followed each time by an aggravation of the nervous symptoms, although the vomiting did not return. We kept her under this management and in bed most of the time until February. A rather marked hydramnios developed about Jan. 15, and an x-ray picture was taken because of the possibility of a monstrosity. This picture showed two normal twin babies, presenting by the breech. Toward term she was allowed to get up for two days but seemed too weak to support much activity. A bag induction was done at term because she did not go into labor and was quite uncomfortable from the hydramnios. The duration of labor which was normal in every way was about eight hours. As soon as the first stage was completed both babies were delivered by breech extraction on February 4, 1928.

This case illustrates the onset of a thyrotoxicosis in a patient who previously had no symptoms of thyroid hyperfunction. It demonstrates the fact that medical management will control certain of these cases, that it is not necessary to terminate the pregnancy if the patient can be kept in bed, and also that Lugol's solution can be used over a period of several months without causing intoxication. This patient while in the hospital was in a rather crowded colored ward with general nursing care, conditions which are not altogether ideal.

One of the babies died shortly after birth due to small cerebral hemorrhages. The other survived, gained normally and had no evidence of goiter and has since developed into a normally healthy child. This is in contrast to the findings of Carlson,[10] who noted distinct evidence of hyperthyroidism in pups and kittens from goiter-bearing mothers.

We wish to record our findings in cases under the above groupings. A review of the data shown in Table I, mild hyperthyroidism, reveals in these cases in general that hyperthyroidism of this degree affects pregnancy very little or not at all. Most of the gestations went close to the estimated term except Case 8, a hydrorrhea gravidarum, and Case 4, a pre-eclamptic toxemia. The babies were all well developed and showed no evidence of thyrotoxicosis. Labor was not complicated. We noted concomitant symptoms of eclamptogenic toxemia in four of the thirteen cases and in two of these there was enough evidence to make a definite diagnosis of pre-eclamptic toxemia. There were eight colored women and five white which is about the usual proportion of entries of these races in the clinic. There were nine multiparae and four primiparae. Considering there is a normal weight increase in pregnancy of twenty-five pounds, there was a loss or a failure to gain normally in all of the nine cases in which the figures were obtained. The thyroid was abnormally enlarged in nine of the thirteen cases. None of these women showed exophthalmos or other eye signs. The urine contained from a trace to 2 plus albumin in six of the thirteen cases. There was no sugar found, which was surprising to us.

Observations on the basal metabolism rate were very carefully made by one of my graduate students, Dr. Busby, who was working on this test in normal pregnant and puerperal women. We were especially interested in comparing the toxic with the normal women as regards basal metabolism rate. We used a Krogh metabolimeter, and from four to eight readings were made on each case on different days. The readings were made after an hour rest period and six hours after a very light meal. All tests were discarded where it was evident the patient was under abnormal mental strain.

It will be seen that the basal rates varied markedly in the different cases. Thus Case 1 had a high reading antepartum of plus 38, a low reading antepartum of plus 16, and eight days postpartum it was 3.5.

TABLE I. MILD HYPERTROPHY

CASE	AGE	RACE	WEIGHT	PARA	GOITER	EXOPHTHALMIC	TOXIC SYMPTOMS	URINE	BLOOD PRESSURE	METABOLIC RATE			BABY	REMARKS
										HIGH	LOW	POSTPARTUM		
1	23	C	122 111	II	None	No	Headaches, dizziness, visual disturbance, edema	Neg.	110/70	+38	+16	+ 3.5 (8da.)	Good 3380 49	
2	23	C		I	Palpable	No	None	Neg.	105/70	+24	+ 8	+ 2.7 (7da.)	2750 47	Puerperal fever
3	26	W		I	Palpable	No	None	Alb. +	128/80	+27.8	+11	0.0 (7da.)	4000 53.5	Prolonged labor
4	20	C	125 142	I	Palpable	No	Edema	Alb. + casts	162/98	+48	+24	+16.0 (6da.) + 8.5 (8da.)	2260 45	Pre-eclamptic
5	18	W	128 144	I	Palpable	No	Headaches Edema	Alb. +	108/38	+55.1	+21.4	+ 1.6 (6da.)	3280 51.5	Overdue 10 days
6	34	C	117 118	III	Palpable	No	None	Neg.	128/75	+48	+18	− 4.0 (7da.)	3220 47	Rapid labor
7	19	C		II	Palpable	No	None	Alb. trace	114/68	+22			2780 42.5	
8	27	W	119 104	III	None	No	None	Alb. ++	104/75	+56	+24		2120 42.5	Hydrorrhea Gravidarum
9	26	C	132 114	IV	Palpable	No	Visual disturbance, edema	Neg.	104/70	+69.3	+54.6	+51.0 (8da.)	3700 50	Pre-eclamptic
10	36	W		IV	Palpable	No	None	Alb. trace	138/85	+39		+30.0 (8da.)	4290 52	Rapid labor
11	26	C	110 111	IV	None	No	Edema	Neg.	100/70	+26	+15	+15.5 (5da.)	2820 48	
12	32	W		II	Palpable	No	None	Neg.	112/85	+24	+14.5	+ 9.0 (5da.)	3270 49	
13	21	C	138 140	II	None	No	None	Neg.	124/80	+37	+25	+ 9.1 (6da.)	2350 45.5	

Case 8 had a plus 69.3 reading as the highest antepartum and 54.6 the lowest antepartum; the eight day postpartum reading was plus 51. This may have been due to an associated mild pre-eclamptic toxemia. The rates in general are rather low, some even well within the normal pregnancy limits, and this corresponds well with the diagnosis of a mild hyperthyroidism. It will be seen that a rate of over 30 was found in eight out of the thirteen cases. Normally in nonpregnant women it is said that a plus or minus 15 is not significant of pathologic hypersecretion. Most observers feel that normal pregnancy may raise the figure to 20 or even 30 but anything above 30 should be considered pathologic.

In those patients showing a basal rate under 25 there were in each case other symptoms upon which the diagnosis of hyperthyroidism was based. Two of the thirteen cases gave evidence of a pre-eclamptic toxemia as well as thyrotoxicosis. We were especially interested in this finding because of the statements of Ward[11] and others that the failure of the thyroid gland to increase its activity during pregnancy is one of the causes of eclamptogenictoxemia. Ward found that the use of saline extract of thyroid, normal human thyroid gland, seemed to affect favorably one case of hyperemesis gravidarum. He also had a patient with exophthalmic goiter who was cured by the injection of an antiserum and two years later became pregnant. She went through pregnancy perfectly normally, and on the fourth day postpartum she developed symptoms of exophthalmic goiter. He feels that the injection of saline extracts of human thyroid glands may favorably alter the metabolism in patients who have eclamptogenic toxemia or hyperemesis gravidarum.

Four of our cases displayed the clinical manifestations of toxic adenoma, Group II. The average age was thirty-one years old and all were multiparae. Two of the four had slight exophthalmos. Two had marked choking sensations and one a marked aphonia and dyspnea on lying down. Two had a 1 plus albumin in the urine and a basal rate of 50, and 105 was noted in two. This test was not made on the other two. Three of the four had symptoms of pre-eclamptic toxemia. All of the babies were born spontaneously and were normal in size and length. Weight loss was noted in one patient of the four. The apparent gain in Case 3 may have been due to pre-eclamptic toxemia with edema. Table II shows the data on these cases.

A consideration of these toxic cases, while few in number, leads us to a more conservative conclusion regarding the coexistence of thyrotoxicosis and pregnancy than that advanced by Gellhorn[12] who concludes that exophthalmic goiter and pregnancy constitute a serious menace for the mother. He believes that girls with a well-developed hyperthyroidism should be advised against marrying. If Graves' disease appears after marriage, conception should be prevented. The

quickest and best method of interruption is by means of a vaginal cesarean section, with tubal sterilization added. We feel that while his view may obtain for the extremely marked cases of exophthalmic goiter and especially if skilled surgical intervention is not available to the patient, we would hesitate in the light of our experience and that of others to advocate the same for all cases, particularly since it is well established that some of these patients are actually benefited by the pregnant state. We are of the opinion that every pregnant woman undergoes a readjustment of the functional activity of the ductless glands. When the readjustment results in a new balance being established, the patient is classified as a normal pregnancy. Various pathologic states may develop from a failure to establish a balance. Given, then, a patient with a disturbed balance before pregnancy begins, an adjustment more nearly to what is considered normal may be established by the pregnancy.

A review of the data in Group III shows five cases classified as exophthalmic goiter. Their average age was thirty years. Three of the five showed marked loss of weight, and four showed moderate exophthalmos. Three showed a slight trace of albumin in the urine, and one had a pressure of 176/96, with headache and epigastric pain and was thought to be a pre-eclamptic toxemia. One patient had a thyroidectomy after which she passed a blood mole. This case was transferred to us from the surgical division after the operation had been done and the abortion was in progress. Three of the five patients entered the ward with the diagnosis of hyperemesis gravidarum. The accompanying clinical manifestation of hyperthyroidism and the basal rate made the diagnosis of hyperthyroidism. Treatment directed at this condition resulted in a marked improvement of the vomiting. The babies were all well developed about term and left the hospital in good condition except one of the twins who died two days after birth in convulsions. Autopsy revealed numerous small hemorrhages in the brain. No abnormalities were noted in the thymus or in the thyroid. There were two colored women and three white women. The basal metabolic rate varied from plus 111 to plus 3 before delivery and was plus 15 and plus 8 after delivery in those cases in which a record was obtained. One of the five cases had not delivered at this writing. Table III shows the results of these cases.

An analysis of the eight cases operated on by Dr. Percy and Dr. Nadeau shows that the average age was twenty-eight years. Three of the eight had considerable loss of weight. Toxic symptoms and enlargement of the gland were present in all. There were none of the symptoms either of hyperemesis gravidarum or pre-eclamptic toxemia. One of the eight cases aborted before leaving the hospital. Four of the cases were diagnosed clinically and histologically as exophthalmic goiter, and three were toxic adenomas. The remaining case was classi-

TABLE II. TOXIC ADENOMA

CASE	AGE	RACE	WEIGHT	PARA	GOITER	EXOPHTHALMIC	TOXIC SYMPTOMS	URINE	BLOOD PRESSURE	METABOLIC RATE			BABY	REMARKS
										HIGH	LOW	POSTPARTUM		
1	28	C	120 145	IV	Enlarged adenoma	No	None	Alb. +	120 80				3240 46.5	None
2	20	C		II	Three times normal	No	Epigastric pain, edema vomiting	Alb. +	134 90				2960 50	Pre-eclamptic toxemia
3	34	W	178 203	IV	Nodular assymmetrical	Slight	Headache edema dyspnea aphonia	Neg.	154 92	+ 50	+39.4	+40 (6 da.) +29.4 (7 wk.) +24.8 (8 wk.)	3260 51	Lugol's after Oct.
4	41	W	216 196	VIII	Bilateral	Slight	Headaches vertigo aphonia epigastric pain	Alb. +	216 196	+105	+47	+26 (8 da.) +23 (7 wk.) + 8.3 (9 wk.)	3660 49	

TABLE III. EXOPHTHALMIC GOITER

CASE	AGE	RACE	WEIGHT	PARA	GOITER	EXOPHTHALMIC	TOXIC SYMPTOMS	URINE	BLOOD PRESSURE	METABOLIC RATE			BABY	REMARKS
										HIGH	LOW	POSTPARTUM		
1	31	W	95 108	II	Moderate firm	Yes	Edema	Alb. +	128 78	+ 53			3220 46.5	Mitral stenosis
2	32	W	160 215	III	Old scar	Mod.	Headache epigastric pain	Neg.	176 95	+ 34			3360 46	Pre-eclamptic
3	37	W	165 133	X	1927 thyroid	No	None	Neg.		+ 3		+ 8	Blood mole	Mitral regurgitation
4	30	C	146 107	I	Moderate	Mod.	Nausea exhaustion	Alb. +	108 52	+111	+20	+15	Twin	Hyperemesis gravidarum
5	22	C	171 129	I	Moderate firm	Mod.	Nervous pulse 140 nausea	Alb. trace	100 54	+109	+12			Not delivered hyperemesis

TABLE IV. CASES OF DRS. PERCY AND NADEAU

CASE	AGE	RACE	WEIGHT LOSS	PARA	GOITER	EXOPH-THALMIC	TOXIC SYMPTOMS	URINE	BLOOD PRESSURE	OPERATION PATHOLOGY	ANESTHETIC	BABY	REMARKS
1	30	W	60	II	Small firm enlarged		Headache	Neg.	144 60	Exophthalmic double lobectomy	Ethylene		2½ months
2	19	W	Sl.	II	Asymetrical soft enlarged		None	Neg.	120 70	Toxic adenoma double lobectomy	Ethylene		4 months
3	37	W	19	VI	Firm enlarged		None	Neg.		Exophthalmic lobectomy	Ethylene local	Miscarried	10 days post-operative miscarried
4	30	W	None	I	Right lobe enlarged nodular	No	None	Neg.	126 72	Toxic adenoma double lobectomy	Local		2 months
5	32	W	35	III	Bilateral enlarged		None	Neg.		Toxic adenoma double lobectomy	Local		6 weeks
6	30	W	Sl.	V	Moderate enlarged		None	Neg.		Exophthalmic double lobectomy	Local	Term twins	5 months toxic in all but 3rd
7	32		Sl.	I	Slight enlarged		None	Neg.		Exophthalmic double lobectomy	Local	Term good	2½ months
8	23			II	Marked bilateral enlarged		None	Neg.		Colloid goiter double lobectomy	Local		4 months

TABLE V. CASES OF DR. SEED

CASE	AGE	RACE	WEIGHT LOSS	PARA	GOITER	EXOPH-THALMIC	TOXIC SYMPTOMS	URINE	BLOOD PRESSURE	OPERATION PATHOLOGY	ANESTHETIC	BABY	REMARKS
1	30	W	30	II	Marked	Yes	Nervousness, dyspnea ascites	Neg.	Normal	Exophthalmic ligation double lobectomy	Local nitrous oxide	Miscarried	6½ months
2	33	W	25	II	Marked	No	Dyspnea, tachycardia	Neg.	Normal	Adenoma double lobectomy	Nitrous oxide	Twins good	3 months

fied as a colloid goiter with toxic symptoms. The basal metabolic rate was not studied in these cases, and I am told by Dr. Percy that he relies very little on this test in handling these cases. The résumé of these cases is presented in Table IV.

A résumé of Dr. Seed's cases is seen in Table V. One was a thirty-year-old white girl who had been in St. Luke's Hospital, Chicago, for two months under medical management. He did a ligation of both superior thyroid arteries in spite of the fact that she was two months pregnant. She was advised to return in a month but waited about the sixth month and entered with marked dyspnea and cardiac decompensation, ascites, and generally poor condition. A right lobectomy was done, and she aborted at six and a half months. A second lobectomy nearly a year later was necessary, and since then she has been normal.

The second case was a thirty-two-year old para ii, with a basal metabolic rate of plus 42. She had had a marked adenomatous goiter with symptoms for several years. A thyroidectomy was done during the third month of pregnancy. She had a smooth postoperative course and delivered twins normally six months later. She lost all goiter symptoms following thyroidectomy.

It is, therefore, seen that on the whole good results are obtained from both the surgical or radical method of handling toxic goiter and the conservative or medical method. It would seem that the medical management should be used in all cases primarily. That the goiter surgeon should be called upon at any stage of the pregnancy to operate when it is evident from the basal rate and the clinical manifestations that the patient is either not improving or at least holding her own. If this intervention can be postponed until viability of the baby, so much the better. From the statistics here given it would seem that local anesthesia is most satisfactory from the surgical standpoint, and as far as contributing to abortion is concerned, it is the ideal anesthesia. The obstetrician should be ready to perform a vaginal or abdominal cesarean section, according to the indications present in the individual case. Teamwork between obstetrician and surgeon is the ideal arrangement and will give the best results.

CONCLUSIONS

From a consideration of these cases it would seem that the following conclusions are justified:

1. Mild hyperthyroidism as judged by the clinical manifestations and the basal metabolic rate is a not uncommon complication of pregnancy, and no special treatment is necessary.

2. Many of the nervous symptoms seen in pregnancy are probably due to abnormal activity of the thyroid gland induced by the pregnant state.

3. Exophthalmic goiter symptoms may manifest themselves first during pregnancy and if present before conception usually are aggravated but may be ameliorated.

4. The vomiting and toxic symptoms of an exophthalmic goiter during pregnancy are apt to be wrongly diagnosed as hyperemesis gravidarum.

5. These patients may best be treated conservatively with bed rest and Lugol's solution, as long as improvement occurs, withholding surgical intervention until it is evident that medical management has failed or, if possible, until the thirty-fifth week when premature delivery following thyroid operation will be harmless to the baby.

6. Operation skillfully performed even in the early months of pregnancy offers a fairly good chance for the baby in exophthalmic goiters and toxic adenomas. Maternal mortalities have been obtained as low as 0.5 per cent, the average maternal mortality being 1 per cent.

7. Toxic adenomas can also be best handled conservatively unless the pressure or toxic symptoms are too severe when lobectomy is indicated.

8. Labor is well supported by these patients, but to spare them as much as possible shortening of the second stage by operative intervention when conditions are favorable is advised.

9. Seriously intoxicated patients first seen late in pregnancy, who do not respond to medical management, may best be delivered by vaginal or abdominal cesarean section.

10. The babies born of mothers who manifested all grades of hyperthyroidism, mild, exophthalmic, and toxic adenoma, showed no clinical evidence of goiter.

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THE RELATION OF BASAL METABOLISM TO GESTATION*

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INTERFERENCE with the reproductive function manifested by menstrual abnormalities, sterility and abortions are so common and the causes so numerous and elusive that any evidence which indicates even one cause, is worthy of our careful consideration.

Examination of the female pelvis is not sufficient. A complete and meticulously conducted study of the woman is necessary and, in the case of sterility, of the husband as well. This requires the cooperation of the gynecologist-obstetrician, the internist and endocrinologist, the genito-urologist, and the laboratory.

In the course of such cooperative investigation during the past seven years we have observed that lowered metabolism is present in a large percentage of cases of menstrual disturbances and sterility and to a definite but lesser proportion of repeated abortions.

In a preliminary report by one of us in 1926 upon *The Relation of Basal Metabolism to Sterility*,[1] attention was drawn to the possibility of deficient metabolism as a cause (or index of a cause) of sterility. Fifty per cent of the sterile women reported had a low basal metabolic rate and of the cases treated with thyroid extract, one-third conceived. One woman of the group became pregnant three times under treatment, bringing the percentage of conceptions to 40.

In that preliminary report the following tentative summary was made: "Definite conclusions cannot be drawn but there is a significance in the findings which demands further investigations to establish the truth or falsity of the possibility that moderate hypothyroidism may be a cause (or index of a cause) of sterility."

Further study and continued experience have convinced us that deficient metabolism does interfere with the reproductive function. "The relation of the thyroid gland to the sex organs is the most ancient and classical interrelation of the functions of the glands of internal secretion. Known to the ancients and a subject of daily gossip, it has passed down through the ages." (Marine.[2])

No new evidence is necessary to prove that the marked degrees of altered thyroid function interferes with the reproductive organs for it is a matter of common knowledge that with both the hyperfunction of exophthalmic goiter and the hypofunction of myxedema, menstrual disturbances are common and conception rare. We have excluded all such cases, for our study is concerned only with the woman with a

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metabolic rate slightly below normal and showing no other signs of myxedema.

It would seem apparent that any deviation from the normal rate must be due to thyroid influence and inasmuch as the patient usually responds to thyroid medication we have used the term "hypothyroidism" in spite of the fact that clinicians in general seem reluctant to attach a diagnosis of hypothyroidism to a patient with low metabolic rate.

Our material was derived from 2,500 consecutive determinations of the basal metabolic rate in all types of patients, of whom 758 had a rate of minus ten or lower. We have studied the women in two groups.

The first group of 137 women includes all the women with low basal metabolism, whose records contained sufficiently accurate data to warrant analysis. The second is a group of 52 sterile women, all with low basal metabolism and all treated with thyroid substance. None of the women in either group showed any other evidence of myxedema. In the first group of 137 women, 78 were married, of whom 35 women or 45 per cent were sterile.

In addition there were 15 cases of relative sterility or cases presenting the following abnormalities: (1) No living children, but one or more stillbirths, miscarriages or abortions (6 cases); (2) one or more living children, but also one or more stillbirths, abortions or miscarriages (9 cases). Sterility, actual or relative occurred, then, in 56 per cent of this series, more than four times the incidence in the United States, according to Lotka[3] who says that sterility occurs in 13 per cent of the white women of the United States.

Forty-four per cent of the 137 women with a low rate had menstrual difficulties: amenorrhea, irregularity, menorrhagia, metrorrhagia, dysmenorrhea, and scanty flow. There was no pelvic condition in any of these cases to account for the symptoms. A goodly percentage of women with abnormal menses are improved by thyroid and hygienic measures, as are also the women who habitually abort, who can be carried through to term.

In the second group of 52 sterile women, 33 or 63 per cent had abnormal menses, 15 or 28.8 per cent had abortions. All of the 52 women with a low basal metabolic rate were treated with thyroid extract upon the supposition that the low rate was due to thyroid influence. Seventeen or 30 per cent of conceptions followed the treatment, one woman becoming pregnant four times and another twice. One woman had twins and two aborted once, giving us as a result of our treatment sixteen babies, a result certainly justifying the treatment.

We believe that the basal metabolic rate should be taken in all cases, when no other cause of sterility can be found, either in the wife or her husband.

SUMMARY

Rearranging the data of the two groups and bringing them up to date (from January, 1928) by the addition of a few recent cases, we find that in 91 cases of sterility, 52 women or 57 per cent had a metabolic rate below normal, of whom 36 per cent had abnormal menses. Thirty per cent of the 52 women became pregnant following treatment, two of them aborted (the treatment having been discontinued after conception), while fifteen of the same group had aborted one or more times before treatment, indicating that the normal metabolic rate should be maintained during pregnancy. It seems to us that the results of our studies leave little room for doubt and we are personally convinced that lowered metabolism, even to a very moderate degree, interferes with the reproductive function.

When we observe that of 137 women with a lowered metabolism, 45 per cent are sterile and of 91 sterile women, 57 per cent have a low basal metabolic rate, it is difficult to escape the conviction that there is a very definite relation between metabolism and the reproductive function.

If the statement be true that the reproductive cells are more subject to deleterious influences than any other cells in the body, our findings are not difficult to understand.

CONCLUSIONS

1. Lowered metabolism, even to a moderate degree, interferes with the reproductive function in a large percentage of cases as is shown by disturbed menses, sterility, and interruption of pregnancy.

2. One-third of all women studied, who had a low metabolic rate and nearly two-thirds of the sterile women with a low rate had abnormal menstruations.

3. Nearly one-half of all the women with a decreased metabolism were sterile and more than one-half of the sterile women had a basal metabolic rate below normal.

4. A little less than one-third of the women with a low rate who conceived, aborted, some of them repeatedly.

5. Restoring the basal metabolic rate to normal by thyroid medication (and hygienic measures), in many cases, improves menstruation, permits conception, and prevents interruption of pregnancy.

6. Therefore, in all cases where no other cause is found for abnormal menses, sterility, and abortions, the basal metabolic rate should be determined and if found low, should be restored to normal by proper treatment.

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DISTURBANCES IN CARBOHYDRATE METABOLISM IN TOXEMIA OF PREGNANCY*

A Partial Answer to the J. Whitridge Williams Questionnaire on Eclampsia†

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SOME time ago Dr. J. Whitridge Williams[1] stated that in order for any theory (of eclampsia) to be regarded as acceptable, it must explain satisfactorily certain pathologic and clinical facts, of which the following may be mentioned: (A) The genesis of the characteristic hepatic lesions; (B) the predisposing influence of primiparity, multiple pregnancy and hydramnios; (C) the disease is more common in northern countries than in the tropics; (D) its incidence increases as pregnancy approaches term; (E) marked edema is usually a favorable sign; while its absence adds to the gravity of the prognosis; (F) true eclampsia rarely occurs, whereas chronic nephritis gives rise to increasingly serious trouble in each succeeding pregnancy; (G) intrauterine death of the fetus is usually followed by improvement and, (H) a milk diet, which is high in protein and mineral constituents, is as efficacious as one low in protein and free of salt.

In addition to these questions I would suggest that explanation should also be made of the following: Under B, that preeclampsia and eclampsia are frequently seen with hydatidiform mole. Under C, that the incidence of eclampsia is increased by sudden changes in the weather. Under D, that convulsions and other symptoms of eclampsia occur in the early weeks of pregnancy in only two conditions; namely, hydatidiform mole and acute yellow atrophy of the liver. Finally to develop a satisfactory theory of eclampsia its etiologic relationship to any similar morbid changes occurring in nonpregnant human beings or in pregnant lower animals should be shown.

GLYCOGEN DEFICIENCY THEORY OF TOXEMIAS

The "glycogen deficiency theory"[2] of the origin of pregnancy toxemias is, in brief, that an insufficient carbohydrate intake in the maternal diet plus the sudden and extraordinary demands of fetal and placental growth and uterine hypertrophy cause a glycogen de-

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ficiency in the body tissues especially noticeable in the liver. This may be either a slowly progressing process or may have acute and even fulminating phases.

The application of the Williams questionnaire to this theory and its supporting facts follow in the ensuing paragraphs in the sequence suggested by Williams and already outlined.

A. GENESIS OF LIVER LESIONS

The genesis of the necrotic liver lesions has been explained as being the result of an excessive glycogen depletion of the hepatic cells, now known to be followed by a fat replacement, tantamount to necrosis. This may be duplicated experimentally by starvation, and is to be seen to a lesser degree in certain of the wasting or "hunger diseases" (Opitz[3]). The earlier stages of this depletion-necrosis have been described as normal or physiologic to pregnancy (Hofbauer[4]). A research now nearing completion in our clinic seems to indicate that to administer to an animal over a period of many days gradually increasing and finally lethal doses of insulin while on a constant diet causes a glycogen depletion with pathologic changes in the liver closely resembling those of the pregnancy toxemias.

Bell[5] states that the necrotic liver lesions seen in pregnancy toxemias do not show the differences in the various clinical types of toxemias which Williams believes to be characteristic of them. That is to say that the necrotic areas are by no means limited to the center of the lobules in hyperemesis and acute yellow atrophy nor to the periphery in eclampsia. Our own work agrees with this.

In summary it may be said that the liver lesions seen in pregnancy toxemias may be imitated experimentally, and that there is open question as to their having distinctive characteristics in the various phases of pregnancy toxemias.

B. INFLUENCE OF PARITY, PLURAL PREGNANCIES, AND HYDRAMNIOS

I have no explanation to offer for the reported predisposing influence of primiparity.

Referring to the second part of this question it is obvious since the glycogen content of the placenta is relatively greater than all other fetal organs, according to McAllister,[6] that the larger the placenta the greater the glycogen drain on the maternal organism.

In multiple pregnancy with double or more the amount of placental tissue the glycogen requirements of two or more fetuses are correspondingly increased, to the mother's detriment.

In syphilis the placenta is proportionately much larger than in normal pregnancies and the relation between syphilis and hydramnios is well known.

It may be added that hyperemesis, as might be expected, is especially common in multiple pregnancies, in syphilitic pregnancies and with hydatidiform mole. In this latter condition there is an enormous hypertrophy of chorionic tissue which must perforce argue a glycogen depletion elsewhere, sufficiently rapid and acute to produce eclampsia in certain instances.

C. GEOGRAPHIC DISTRIBUTION OF ECLAMPSIA

A ready explanation of the comparative rarity of eclampsia in the tropics is that in tropical countries the diet is predominatingly carbohydrate as compared to that of northern countries. It will be remembered that in Germany during the War, the incidence of eclampsia was noticeably diminished, according to Gessner[7] and others. This was attributed to the increase in the consumption of carbohydrate foods and the general lack of meat in the war-time diet of the civilian population.

On the other hand the incidence of eclampsia among the Esquimaux is not excessive,[8] the reason for this being readily comprehended. Traders now supply even the natives of the outlying Arctic regions with canned vegetables and fruits, but even among those tribes whose diet is still almost entirely meat or protein, the continued cold and the freedom from sudden changes in the weather prevent the unexpected metabolic upsets common to quick changes in body-heat requirements.

Eclampsia is most common in the temperate zones which are subject to all degrees of sudden changes in external temperatures, especially in the Spring and Fall. This zonal frequency and the seasonal incidence of eclampsia may reasonably be explained by certain observations of Embden, Lutze, and Lufman.[9] "There is an increase in blood sugar in cold weather and a corresponding decrease in warm weather under similar conditions of food intake or nourishment. Metabolic rates are normally increased in cold weather and decreased in warm weather to satisfy the body heat requirements in response to external temperatures." Increased metabolism to increase body heat means increased consumption of glycogen as fuel and thus is an additional drain on the reserves. Abrupt changes in the weather might therefore readily initiate the fluctuations in blood sugar which we have shown to be characteristic of eclampsia,[10] and we already know that such weather changes do increase the incidence of eclampsia.[11, 12]

A pregnant woman whose metabolic balance has already become dangerously unstable by reason of a dietetic insufficiency might require nothing more than a sudden cold spell to upset it completely. The influence of weather changes on the incidence of hyperemesis is also noticeable.

D. ECLAMPTIC TOXEMIA A DISEASE OF LATE PREGNANCY ONLY?

The fetal requirements naturally increase as growth proceeds and physiologic resistance to this drain may be lessened as time goes on. We[10, 13] have previously suggested that the chief difference between the clinical symptoms of the toxicoses of early and of late pregnancy is due to the fact that the former is a slow, and the latter an acute, rapidly progressing process. In early pregnancy the fetal requirements are less and the demands are more gradual so that the glycogen depletion of hyperemesis which has been demonstrated[13] rarely is swift enough to cause convulsions. Occasionally, however, we see that fulminating process termed acute yellow atrophy of the liver which is pathologically identical with hyperemesis but is so acute that eclampsia-like convulsions usually occur. Thus, there is afforded a connecting link between the toxemias of early and late pregnancy.

Hydatidiform mole in which hypertrophy of fetal (chorionic) tissue goes on at a rate many times more rapid than that of usual fetal growth is frequently able to develop typical eclampsia in the third or fourth months of the gestation. In other words if conditions of late pregnancy are simulated eclampsia may occur in the early weeks of pregnancy.

E. THE FAVORABLE SIGNIFICANCE OF EDEMA

Marked edema with nephritis from any cause is now conceded to be a protective measure. Clinicians in general state that the toxins which collect in an attack of acute nephritis are diluted by edema in the tissues and that the prognosis is thereby made more favorable. Therefore this is not peculiar to eclampsia.

F. RELATIONSHIP BETWEEN ECLAMPSIA AND CHRONIC NEPHRITIS

The investigations of Harris[14] on eclamptic women after delivery at the Johns Hopkins Hospital show that an attack of eclampsia does not leave their kidneys as entirely unimpaired as was previously supposed.

May it not be that these kidney conditions are relative and that pre-existing chronic nephritis makes a predisposition and increasing susceptibility to such trouble during each pregnancy? A woman who survives an attack of true eclampsia may then go through subsequent pregnancies with the help of the better prenatal care which she must seek and demand after such an experience unless she is totally benighted. Do we know however that she has not become a potential nephritic? Harris' findings indicate that she often does and these states therefore may be thought of as being related rather than divorced as originally suggested.

H. APPARENT FALLACIES IN DIETETIC TREATMENT

Recent investigations of Harding and Van Wyck[15] seem to indicate that a high protein diet is not as serious in these states as was previ-

ously thought. My coworkers and I have long believed that a protein diet is not so damaging by direct "irritation" as it is by what it lacks. Finally it should be pointed out that a milk diet even though high in protein is also high in sugar content and therefore should be efficacious according to our theories.

POSSIBLE SIMILARITY OF ECLAMPSIA TO OTHER DISEASES

In reply to our own final question as to a relationship between pregnancy toxemias and similar conditions in the nonpregnant or in animals, it may be said that eclampsia resembles "acute yellow atrophy of the liver" in the nonpregnant and that this too shows a hypoglycemia; that eclampsia and hypoglycemia from insulin overdosage are extraordinarily alike, and that the toxic symptoms of the latter may be produced (John[16]) as are eclamptic convulsions at any level of blood sugar from 200 mg. or more down if this level has been suddenly reached and follows an overdosage of insulin given at a still higher level ("relative hypoglycemia");[10] that the experimental extirpation of the liver in dogs (Mann and Magath[17]) closely resembles a true eclamptic state; that both dogs and cows are said by veterinarians to have diseased states closely resembling eclampsia in humans. In connection with this latter it is interesting to note that Widmark and Carlens[18] have made a study recently of parturient paresis in cows. Williams[19] has referred to the opinions that this is a disease of lower animals closely resembling eclampsia. These authors now find it to be a lactation hypoglycemia, immediately relieved by intravenous injections of dextrose, the same treatment suggested empirically by me in 1920 for eclampsia.

The usual effective treatment of parturient paresis, namely, injection of air into the udder may reasonably owe its efficacy to the pressure which temporarily checks lactation with its sudden drain of body sugar.

COMMENT

Under no circumstances would I wish to be misunderstood as saying that the carbohydrate deficiency or glycogen depletion theory is a completely satisfactory or full explanation of the origin of pregnancy toxemias. Obviously such conditions are complex affairs and probably no one simple explanation can ever be found to account for them fully. I maintain merely that to class pregnancy toxemias as being associated with depletion of the body stores of glycogen and secondary hypoglycemia, explains more fully and more consistently the vagaries of these complex states than has been done heretofore.

It is unfortunate that Zweifel should have dubbed eclampsia the "disease of theories." In the face of such a term one feels considerable temerity at advancing any further theories, yet it is only by the

development of strong convictions to be persistently investigated, weighed, and criticized that the mystery of these conditions will ever be solved. I have no feeling of apology for having become so engrossed in the study of pregnancy toxemias for these past ten or twelve years, nor do I believe that anyone who does likewise has the presumption to believe that he alone can solve something which so many others have failed to elucidate. The fascination of the study of this complicated disease is sufficient reward even if there are no other results.

My attempt to apply these ideas to Dr. Williams' questionnaire has not been in the conceit that they supply the full answer. On the contrary it has been done merely in an effort to see wherein the fabric which I have been trying to weave fails to cover the splendid and thoughtful pattern laid down by Dr. Williams.

If by pointing out these deficiencies this paper supplies a few suggestions for further research it will have been warranted.

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INFECTION IN THE PUERPERIUM, WITH ANALYSIS OF 8000 CASES*

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WE ALL realize that puerperal infection remains one of the great problems for the obstetricians to solve. It is true that it is recognized as being a preventable infection, but this is not absolutely true and it still remains one of the two great causes of maternal mortality and of a morbidity the extent of which cannot be calculated. It is generally considered to be an infection which is introduced from without at or near the time of delivery. This is doubtless true in most instances. Yet, there seem to be a few cases where virulent organisms are harbored within the genital tract of the individual and still others, rare perhaps, where the offending organism is deported from some more remote tissue to lodge in or around the recently traumatized and weakened genitalia.

Granting the impossibility of not unintentionally and occasionally exposing the mother to these infectious agents by either the exogenous or endogenous route, we have still failed to solve the problem in its entirety. Results indicate that it is not possible to infallibly protect groups of mothers from the danger of infections which at times become serious and too often fatal. There are obviously other factors at work. It happens too frequently to be accidental that one woman with a normal uncomplicated delivery becomes infected while another, confined at nearly the same time, in almost the same environment, but delivered operatively, remains free from infection. Why should one woman without operative manipulation die from a rapidly fatal infection while another acquires a slight infection or one which runs a mild course to recovery? Is this all to be attributed to a difference in the virulence of the infecting organism and to variations in aseptic technic, or is it in part due to the resistance and immunity of the woman? Undoubtedly both factors are of enormous importance, but greater consideration has been given to a study of the various bacteria which infect these mothers and to the development of aseptic care than has been manifested in the other side of the picture.

It is well known that there are many racial and individual immunities to different diseases. These are of course both natural and acquired. It is useless and unnecessary to go into the details of this

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*The complete paper cannot be included here for lack of space. It will be published in full in the current volume of the Association's transactions and in the author's reprints.

general problem at this time, but it may be interesting to note some peculiarities in relation to certain diseases with which the streptococcus is definitely recognized as being associated. One of the diseases is scarlatina, which is usually quite definitely recognized and ordinarily remembered by the patient. This disease generally confers immunity against a subsequent attack. Why might it not confer more or less immunity to a later occurrence of a puerperal infection with streptococcus, which is the most frequent and dangerous agent of this disease, as well as to other streptococcic infections?

Hofbauer[1] has been studying the local defense mechanism and your President, Dr. Palmer Findley,[2] called attention to this field of endeavor two years ago in his presentation "The Biologic Defense in Puerperal Infection." Dr. Arthur L. Bloomfield[3] has been studying "The Association of Susceptibility to Scarlet Fever and Acute Tonsillitis" and draws the conclusion that certain people possess a natural or at least unexplained resistance to hemolytic streptococcic infection of the lymphadenoid tissue of the throat. There is a significant positive association between susceptibility to two types of infection of this sort, acute follicular tonsillitis, and scarlet fever.

Geller,[4] in his study of the bactericidal power of the blood in pregnancy and the puerperium, found a decided rise in the bactericidal index during the twenty-four hours following delivery. He regards this of special significance because it occurs at a time when the antibodies and the cellular defense, or so-called granulation wall, have not yet developed. He recognizes that other factors may play an even more important rôle.

In a study of streptococcic diseases and their prevalence in Illinois[5] during the past seventy-five years, one is struck by an apparent relationship between the incidence of a group of diseases known or suspected of being due to infections with the streptococcic group of organisms. The diseases considered in this analysis are erysipelas, scarlet fever, septicemia, and rheumatism. In early days these diseases were very prevalent and in many instances they assumed epidemic proportion in various communities with higher fatality rates than at the present day. One of the significant improvements in the last half century is the lessened prevalence and lowered virulence of most members of this group. The Illinois death rates from scarlet fever have declined from 98.7 per 100,000 of population in 1860 to 11.5 in 1890, and those of Chicago from a rate of 114.7 to 16.1 for the corresponding years. The rate for the years[6] 1919 to 1925 was 3.0 for Illinois and that for Chicago was the same.

In Minnesota[6] the mortality rate for 100,000 inhabitants for scarlet fever was 6.0. This covers a period of seven years, from 1919 to 1925. The rate in Minneapolis for the years 1925 and 1926 was five and six respectively.

It is commonly said that there has been no decrease in the mortality rate from puerperal fever. This may be correct for the past twenty or twenty-five years, but it is not true if a longer period is covered as it shows a downward trend corresponding to other streptococcic diseases.

These results are common experiences as are seen from Table I, which gives some data relative to scarlet fever and erysipelas. It is interesting to note, however, that there has not been in recent years the same downward trend with reference to puerperal septicemia as is noticed in the other two diseases. A similar condition is shown in Table II, in which the rates for scarlet fever and puerperal septicemia are compared. In Table IV a similar situation is revealed, and in addition a comparison is made between the rates of scarlet fever and puerperal infection for the colored and white population.

There seems to be a definite difference in the susceptibility of the white and colored races to scarlet fever and puerperal septicemia. This is shown in Tables I and IV. The mortality among the colored

TABLE I. MORTALITY RATES FROM SCARLET FEVER, ERYSIPELAS, AND PUERPERAL SEPTICEMIA PER 100,000 ESTIMATED POPULATION FOR WHITE AND COLORED PERSONS, U. S. DEATH REGISTRATION AREA, 1910-1925 (8)

YEAR	SCARLET FEVER			ERYSIPELAS			PUERPERAL SEPTICEMIA		
	TOTAL	WHITE	COLORED	TOTAL	WHITE	COLORED	TOTAL	WHITE	COLORED
1910	11.6	12.0	3.4	4.5	4.6	4.0	7.2	7.0	13.1
1911	8.9	9.2	1.5	4.2	4.3	2.9	7.4	7.1	13.3
1912	6.7	6.9	1.6	3.8	3.9	2.5	6.5	6.2	12.4
1913	8.7	9.0	2.9	4.0	4.1	2.3	7.2	7.0	11.4
1914	6.6	6.9	1.5	3.8	3.9	2.0	7.1	6.8	13.1
1915	3.6	3.7	1.2	3.5	3.6	2.1	6.3	6.0	10.7
1916	3.3	3.5	1.1	3.8	3.9	1.8	6.7	6.4	10.8
1917	4.2	4.5	0.8	3.8	4.0	2.0	6.9	6.6	11.9
1918	3.0	3.3	0.4	3.2	3.3	1.7	6.5	6.0	11.7
1919	2.8	3.0	0.5	2.6	2.7	1.2	5.8	5.4	10.5
1920	4.6	4.9	0.8	3.1	3.2	1.7	6.6	6.2	11.7
1921	5.3	5.7	1.1	2.8	2.9	1.5	6.8	6.3	11.5
1922	3.5	3.8	0.7	2.5	2.6	1.0	5.7	5.2	10.4
1923	3.5	3.8	0.9	2.7	2.8	1.1	5.8	5.4	10.4
1924	3.1	3.4	0.6	2.5	2.6	1.3	5.8	5.2	11.1
1925	2.7	2.9	0.7	2.4	2.5	1.3	5.5		

people is definitely less than among the white people for both scarlet fever and erysipelas. This is especially noticeable in the former disease. It seems to be generally recognized among those who come in contact with the colored race that they are less susceptible to infection with scarlet fever than are the whites.

Doull,[7] in discussing the incidence of measles, scarlet fever, diphtheria, and so forth, in Brazil notes marked variations in the mortality from scarlet fever in the northern and southern states of the United States. It is definitely greater in the northern than in the southern states, which is possibly due to the large number of negroes in the latter. The situation is reversed when one compares the mortality of the two races from puerperal septicemia, the mortality among the

negroes from this disease being almost twice as great as among the whites. One might argue that this is due to greater exposure to infection on account of poorer obstetric care among the negroes. The experience of those conducting clinics where both whites and blacks are admitted seems to indicate that the latter are more susceptible to puerperal sepsis. It is interesting also to note the trend of these diseases during recent years. In the past fifteen years the general mortality rate from scarlet fever has been markedly reduced for both whites and blacks in the Death Registration Area as shown in Table I. That this reduction is almost world-wide is shown in Table II. The same prog-

TABLE II. COMPARATIVE DEATH RATES FROM PUERPERAL SEPTICEMIA AND SCARLET FEVER IN VARIOUS COUNTRIES (9-10)

	DEATHS FROM PUERPERAL SEPTICEMIA PER 10,000 LIVE BIRTHS					DEATH RATE FROM SCARLET FEVER PER 100,000 POPULATION		
COUNTRY	1921	1922	1923	1924	1925	1901-1905	1911-1915	1921-1925
Australia	15	14	17	20	17	7	3	3
Belgium	24	21	29	31	28	42	46	14
Canada (birth reg. area)	11	11	18	17	17	41	19	16 (Ont.)
Chile	24	22	19	13	15	5	3	3
Czechoslovakia	—	12	15	12	14			
Denmark	13	9	10	9	9			
England and Wales	14	14	13	14	16	39	21	11
Germany	28	28	30	29	26	62	38	7
Hungary	13	13	13	15	14	189	162	70
Irish Free State	—	—	19	16	17			
Northern Ireland	—	19	16	15	16	15	29	9 (Ireland)
Japan	13	12	13	13	10			
The Netherlands*	7	7	6	7	9	8	7	3
New Zealand	17	18	19	19	15	16	5	3
Norway	8	7	7	6	—	14	11	1
Salvador	10	11	10	8	9			
Scotland	20	20	19	17	16	27	43	27
Spain	32	32	28	27	—	34	24	16
Sweden	13	11	—	—	—	28	16	9
Switzerland	31	25	22	16	20	17	8	3
Uruguay	19	16	17	16	15	28	2	1
U. S. birth registration area	27	24	25	24	24		8.9—3.6	5.3—2.7

*Prior to 1924 live-born infants who died before registration of birth (within three days of birth) are omitted in calculating the maternal mortality rate.

ress toward prevention is to be noticed with reference to erysipelas as applied to both whites and negroes. This trend downward is doubtless due to better quarantine regulations and other means of prevention. This same improvement is not noticeable with reference to puerperal septicemia. There is some downward trend shown in Table I, but this is a rate per 100,000 population and is in part at least accounted for by a diminution in the birth rate. The same improvement is not noticeable in tables based on the rate for living births for either the United States or other countries (Tables II and III).

One cannot but wonder why there should be no material reduction in the mortality from puerperal sepsis along with the general improve-

ment in health conditions and the lessened mortality from other streptococcic diseases. Is it because there has been no general improvement in obstetric care? Can it be possible that such infection has been reduced to the lowest possible level? Are there perhaps some factors which are being overlooked?

It seems to be true that the negroes have a relatively high natural immunity to scarlet fever and erysipelas as compared with the whites. This does not seem to be true with reference to puerperal sepsis. Do

TABLE III. DEATH RATE FROM PUERPERAL CAUSES PER 1,000 LIVE BIRTHS, WHITE AND COLORED, BY STATES AND YEARS (8)

	PUERPERAL SEPTICEMIA						OTHER PUERPERAL CAUSES					
	1919	1920	1921	1922	1923	1924	1919	1920	1921	1922	1923	1924
Kentucky												
White	3.2	2.5	2.6	2.4	2.2	2.5	3.8	3.5	3.0	3.0	3.3	3.2
Colored	6.0	7.0	7.0	9.4	7.7	7.1	6.4	6.0	7.7	9.1	7.7	6.0
Maryland												
White	2.4	1.8	2.0	1.6	2.0	2.5	5.3	4.8	3.9	3.7	3.4	3.1
Colored	4.0	5.0	3.7	3.6	2.9	5.5	7.5	6.8	5.9	4.8	5.4	4.6
Mississippi												
White	–	–	2.2	1.8	2.1	1.8	–	–	4.9	4.6	4.4	4.7
Colored	–	–	4.0	3.6	3.8	4.0	–	–	8.0	6.5	7.1	8.5
N. Carolina												
White	1.5	1.7	1.4	1.6	1.4	1.6	6.7	6.9	4.7	5.5	5.3	5.0
Colored	2.9	3.1	3.0	2.8	2.6	2.8	8.9	10.1	7.2	7.2	8.1	7.6
S. Carolina												
White	1.8	1.8	1.7	1.8	1.4	2.0	6.0	7.1	6.0	6.8	6.0	5.6
Colored	4.5	3.7	3.4	4.5	2.9	3.2	9.9	11.7	8.4	8.3	9.3	10.9
Virginia												
White	1.5	1.9	1.8	1.6	2.0	1.9	5.1	5.6	3.9	4.3	4.0	3.1
Colored	3.3	3.1	3.5	3.6	3.1	3.1	8.6	8.0	6.4	6.5	7.7	6.9

fewer blacks acquire immunity to streptococcic disease which may be inoculated as in puerperal sepsis or is there a difference in the infecting organism? Perhaps there are a multiplicity of factors which are difficult to determine.

That there is a definite difference between the mortality rates of the two diseases for whites and blacks is shown in Tables I and III, where the rates are compared for puerperal sepsis and scarlet fever among the two races. It is readily seen that the mortality rate from puerperal sepsis is quite uniformly greater in each state for the negroes than for the whites. The reverse is true for scarlet fever, which has a constantly lower mortality rate in every state for the colored than for the white race. In order to bring out a little more clearly some points, Table IV was compiled to show comparative rates for some other acute infectious diseases. The mortality rate of typhoid fever is definitely greater for the negroes than the whites. This is probably due to the greater incidence of this disease from poorer sanitation though the difference in the care and treatment might be a contributory factor. It is further possible that the white race might have a greater natural immunity to this disease. Measles present a varied picture and show

no constant difference in the rates, indicating probably that there is no racial immunity to this disease. The comparison of measles and scarlet fever is important because it points to the fact that the exanthemas are not overlooked in the colored race. At least measles are quite definitely diagnosed as a cause of death among negroes in as great frequency as in the whites. It is unlikely that erysipelas as a cause of death would be frequently overlooked and yet the mortality rate is definitely lower for the negroes than for the whites, as is shown in Table I. It seems to be true that statistically at least the colored race has a greater resistance to two of the streptococcic diseases than the white race of the United States.

TABLE IV. CRUDE MORTALITY RATES FROM TYPHOID, MEASLES, SCARLET FEVER, PUERPERAL SEPTICEMIA, AND OTHER PUERPERAL CAUSES (8)

YEAR	CRUDE RATES PER 100,000 POPULATION						CRUDE RATES PER 100,000 FEMALE POPULATION			
	TYPHOID		MEASLES		SCARLET FEVER		PUERPERAL SEPTICEMIA		OTHER PUERPERAL CAUSES	
	WHITE	COLORED	WHITE	COLORED	WHITE	COLORED	WHITE	COLORED	WHITE	COLORED
1920	6.6	19.7	9.3	4.1	5.0	0.8	12.4	23.0	23.6	43.6
1921	7.7	22.6	4.3	3.4	5.8	1.1	12.8	23.3	18.7	37.0
1922	5.7	20.2	4.7	3.0	3.9	0.8	10.5	20.7	18.4	35.9
1923	5.4	17.9	10.5	15.7	3.8	1.0	10.9	20.9	17.7	38.0
1924	4.9	21.8	7.1	14.7	3.4	0.7	10.5	22.5	17.1	42.5
1925	6.0	25.8	2.4	1.9	2.9	0.8	9.9	22.5	16.4	41.9

The greater incidence and higher rate for puerperal septicemia among the blacks are equally apparent and are accompanied by a disproportionately, even higher mortality rate from other puerperal causes. This of course indicates that they have a higher percentage incidence of obstetric complications or that they receive poorer care, both of which are probably true. It is unlikely that deaths among the colored would be more completely and accurately reported than those among the whites. Table V shows practically the same data as Table IV, except that the actual number of deaths is given as well as the rate per 100,000 females.

In a recent discussion of puerperal infection before the American Gynecological Society, Dr. C. Jeff Miller was of the opinion that the pure black was a better surgical risk and withstood infection better than the whites, but that the mulatto was a poorer risk. Dr. J. W. Williams reported some recent work from the Johns Hopkins Clinic indicating that puerperal infection is about twice as frequent in the negroes as in the whites. They have also made the observation that the whites are more susceptible to the hemolytic streptococcus and less to the anaerobic nonhemolytic to which the negro seems much more susceptible. If correct, this could explain the greater resistance of the blacks to scarlet fever and their increased susceptibility to puerperal infection with the anaerobic nonhemolytic streptococcus, with which variety they seem to be more frequently infected.

TABLE V. PUERPERAL MORTALITY RATES PER 100,000 FEMALE POPULATION FOR WHITE AND COLORED PERSONS, U. S. A. DEATH REGISTRATION AREA, 1920-1925 (8)

YEAR	PUERPERAL SEPTICEMIA						OTHER PUERPERAL CAUSES					
	NUMBER ALL AGES			CRUDE RATE PER 100,000 FEMALE POPULATION			NUMBER ALL AGES			CRUDE RATE PER 100,000 FEMALE POPULATION		
	TOTAL	WHITE	COLORED	TOTAL	WHITE	COLORED	TOTAL	WHITE	COLORED	TOTAL	WHITE	COLORED
1920	5800	4984	816	13.3	12.4	23.0	10,976	9334	1642	25.3	23.6	43.6
1921	5881	5048	833	13.7	12.8	23.3	8,681	7356	1325	20.2	18.7	37.0
1922	4928	4180	748	11.3	10.5	20.7	8,626	7331	1295	19.8	18.4	35.9
1923	5156	4397	759	11.7	10.9	20.9	8,549	7164	1385	19.4	17.7	38.0
1924	5134	4305	829	11.5	10.5	20.7	8,589	7022	1567	19.2	17.1	42.5
1925	5018	4172	846	10.9	9.9	22.5	8,463	6888	1575	18.5	16.4	41.9

One might conclude from a consideration of Tables I to V that there has been a downward trend of some diseases which may be considered as due to infection with the streptococcus. This is quite definitely shown statistically in Table I for scarlet fever and erysipelas. In Table I there is an apparent decrease in the mortality from puerperal septicemia per 100,000 population, which also appears in Table IV per 100,000 female population. This decrease is not so apparent in Tables II and III where the rate is based on live births. One reason for this would be that the number of births has been rather rapidly decreasing. In any case the decrease in mortality from puerperal septicemia has been very slight as compared with erysipelas and scarlet fever, especially the latter. One is struck by certain racial differences when comparing the mortality rates of the whites and blacks from certain diseases. This appears very definitely in Table I. It is interesting to note the striking differences in scarlet fever; the rate has steadily decreased for both races but has retained about the same ratio, always being much less for the negro. The same is true with reference to erysipelas, though the difference in the rates is not so striking. The exact opposite holds true with reference to puerperal septicemia, which has a constantly and more or less uniformly higher rate among the blacks than the whites. There has been a slight proportional decrease in this rate for both races. One might ask if this were due to a difference in the resistance of the two races or to greater exposure to infection of the negroes, from either poorer care or more frequent complications. In Tables III and IV it is easily seen that the mortality rate is much higher among the negroes from other puerperal causes, which of course includes some other infections than puerperal septicemia. This points probably to more complications and poorer obstetric care. In Table III one sees in all the states uniformly higher rates for the blacks than the whites, indicating that it is not a local or accidental condition. In Table IV certain other diseases are compared and indicate racial susceptibility or the existence of conditions more favorable to infection. In Table II an attempt is made to ascertain whether or not there is any association between a high rate for puerperal septicemia and one for scarlet fever. In comparing these mortality rates for different countries there seems to be no constant relationship. Belgium, Germany, and Spain show rather high rates for both puerperal septicemia and scarlet fever. On the other hand, The Netherlands and Norway show low rates for both diseases. Australia and Chile show low rates for scarlatina and a moderately low one for puerperal septicemia. There does not seem to be the same tendency in the white race to have a low mortality rate for scarlet fever associated with a high rate for puerperal septicemia. In Table V the same comparative points are brought out with reference to puerperal deaths among the white and

colored races, and in addition the actual number of deaths is given so that one may obtain some idea of the number of persons involved.

It is desirable to secure if possible more definite information as to whether or not a resistance may be built up against puerperal septicemia of streptococcic origion. Scarlet fever, inasmuch as it seems to be a streptococcic disease which establishes immunity to subsequent attacks, might build up such a resistance.

It seemed of some importance to analyze a large group of puerperal cases with reference to the incidence of scarlet fever and the relationship to febrile puerperia and to fatal cases of puerperal septicemia. We have analyzed two such groups of cases, one consisting of over 6000 cases from the Minneapolis General Hospital and the other from private practice, made up of 2000 cases. This makes a combined series of over 8000 cases. In the Minneapolis General Hospital group of 6060 cases, there were 723 cases with a history of scarlet fever, or a percentage incidence of 11.9. In the private series of 2000 this disease occurred in 380 instances, or 19 per cent. This totals 1103 cases, or 13.6 per cent, for the entire series. The general incidence of scarlet fever seems to be between 11 and 12 per cent. The figures and percentages for those not having scarlet fever represent the difference and appear in Table VI. This table also shows an analysis of the febrile and afebrile cases in both those with and without a history of scarlatina. A temperature of 100.4° F. or more on two or more days during the puerperium was taken as the standard of a febrile puerperium. Percentages and rates were computed for each group and subgroup on the basis of the total number of cases and also of those in each subgroup. It is interesting to note that a very much higher percentage of cases without scarlet fever had a febrile puerperium than of those who had a history of this disease. This is marked in both groups of cases as well as in the entire series. In this same table the cases are also divided into afebrile and febrile groups and each of these is subdivided into those with and without a history of scarlet fever. The percentages were figured on the same basis as has been described. We find a higher percentage incidence of febrile puerperia among those without scarlet fever than corresponds to the general incidence of this disease. In the Minneapolis General Hospital group 88 per cent had no history of scarlet fever but over 90 per cent of the febrile cases fall in this group. The same is true in the private series of cases, but more marked, as the relative percentages were 81 and 92. For the entire series, then, the percentage incidence of cases without scarlet fever was 86.3 and the percentage of febrile cases in this whole group was 90.7. The reverse is true for those who had scarlet fever. This seems to indicate that a greater percentage of cases have a febrile puerperium in those who have not had scarlatina than in those who have had the disease.

TABLE VI. ANALYSIS OF CASES SHOWING RELATION OF FEBRILE PUERPERIUM TO INCIDENCE OF SCARLET FEVER

	WITH SCARLET FEVER						WITHOUT SCARLET FEVER					
	AFEBRILE		FEBRILE		TOTAL		AFEBRILE		FEBRILE		TOTAL	
	NO.	RATE[1]	NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE
M.G.H.[2] 6060	651	10.8 90.0	72	1.1 10.0	723	11.9 100.0	4668	77.0 87.5	669	11.0 12.5	5337	88.0 100.0
Private 2000	363	18.15 95.5	17	0.85 4.5	380	19.0 100.0	1422	71.1 87.8	198	9.9 12.2	1620	81.0 100.0
Combined 8060	1014	12.5 91.9	89	1.14 8.1	1103	13.6 100.0	6090	75.5 87.5	867	10.7 12.5	6957	86.3 100.0
	AFEBRILE						FEBRILE					
	WITH SCARLET		WITHOUT SCARLET		TOTAL		WITH SCARLET		WITHOUT SCARLET		TOTAL	
	NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE
M.G.H. 6060	651	10.8 12.2	4668	77.0 87.8	5319	87.7	72	1.2 9.7	669	11.0 90.3	741	12.2
Private 2000	363	18.15 20.3	1422	71.1 79.7	1785	89.2	17	0.85 8.0	198	9.9 92.0	215	10.7
Combined 8060	1014	12.5 14.3	6090	75.5 85.7	7104	88.1	89	1.1 9.3	867	10.7 90.7	956	11.8

[1]Rate per 100 cases. Upper figure is rate for total cases, lower figure for group cases.
[2]Minneapolis General Hospital.

In Table VII a study is made of both the febrile and the fatal cases. It is apparent that the rate for febrile cases is definitely higher in those cases who give no history of scarlet fever than in those who have had it. The number and rates are given with reference to fatal cases. All cases who died of any infection in connection with labor or the puerperium are included. Two cases are also incorporated from whom no history was obtainable, as they entered the hospital in a critical condition and died before a complete history could be obtained. Abstracts of the fatal cases are appended so that their character may be better appreciated.

There were 23 in all, of which two are eliminated from the group statistics because of the absence of a history. This leaves 21 cases for closer analysis. Of these cases, two gave a history of scarlet fever, Cases 5 and 22. The former had a pyelitis and probably a puerperal sepsis. The records of bacteriologic study are incomplete and no autopsy was permitted. The other case was a preeclamptic who had evidence of a respiratory tract infection at the time of delivery and died later of a lobar pneumonia. Of the ten cases with known streptococcic infections, not one gave a history of having had scarlet fever. It would appear, then, that scarlet fever might confer some immunity to subsequent infection with streptococcus during the puerperium. In considering the prevention of puerperal septicemia the various antiseptic and aseptic technics have been used with success in limiting puerperal infections. Bacteriologic studies have been made to determine the various organisms responsible for this condition. There still remains a residuum of cases which become infected and die from puerperal sepsis. Perhaps we can improve our morbidity and mortality rates by more extensive investigation of the factors in the resistance to disease. As pointed out earlier in this paper, such investigation has recently been carried out and is still being conducted. Scheyer[11] has carried out experiments to determine the part played by the reticuloendothelial system in combating streptococcic infections. He believes that the cells of this system show that certain individuals have no reaction against streptococcic infections, that others react but have their resistance soon overcome, and lastly, others who perhaps as a result of previous streptococcic infection are immune or very resistant to it. Burt-White[12] has recently reported some work on the skin test for sensitiveness to streptococcic toxin. He reports 100 tested cases, of which twenty-seven were toxin-sensitive and seventy-three were not. Eight, or 30 per cent, of the twenty-seven women had a morbid puerperium. Only two of the seventy-three women exhibited morbid puerperia. He concludes, "women who react positively to intradermal inoculation of scarlatinal toxin are more liable to develop puerperal sepsis than nonreactors."

Hacket made some skin tests on some of our patients at the Minne-

TABLE VII. INCIDENCE OF FEBRILE AND FATAL CASES OF INFECTION WITH AND WITHOUT A HISTORY OF SCARLET FEVER

CASES	FEBRILE CASES								FATAL CASES					
	WITHOUT SCARLET FEVER			WITH SCARLET FEVER			TOTAL		WITHOUT SCARLET FEVER		WITH SCARLET FEVER		TOTAL	
	NO.	FEBRILE	RATE[1]	NO.	FEBRILE	RATE	NO.	RATE	NO.	RATE	NO.	RATE	NO.	RATE
M.G.H. 6060	5337	669	11.0 12.53	723	72	1.2 9.95	741	12.2	16	0.29 2.38	1	0.14 1.4	19 17(2)	0.31 2.29
Private 2000	1620	198	9.9 12.22	380	17	0.85 4.5	215	10.7	3	0.18 1.51	1	0.27 5.8	4	0.2 1.86
Combined 8060	6957	867	10.7 12.5	1103	89	1.1 8.1	956	11.8	19	0.27 2.19	2	0.18 2.25	23 21(2)	0.21 2.2

[1]Rate per 100 cases. Upper figure is rate for total cases, lower figure for group cases.

apolis General Hospital and found among 161 patients sixteen questionable, 102 negative, and forty-three positive reactions to streptococcic or scarlatinal toxin. Of the 145 cases reacting definitely, 29 per cent were toxin-sensitive. There was a positive history of scarlet fever in twenty-one of the 145 cases, or 14.5 per cent. Fifteen were in the nonreacting group, a percentage of 10.3 of the whole series and of 14.7 of the group. Six were toxin-sensitive, a percentage of 4.2 for the series and of 13.9 for the group. Among the sensitive cases there were six with a febrile puerperium, which is a percentage of 4.2 for the series and 13.9 for the group. In the nonreacting group, thirteen had a febrile puerperium, which makes 9 per cent of the total and 12.7 per cent for the group. There were no fatalities from infection in this series.

This is a small series and it is impossible to draw any conclusions, but a slightly smaller percentage of the nonreacting cases showed some evidence of infection in the puerperium. The incidence of scarlet fever is somewhat higher than in our larger series of cases. A percentage of 71 of those having had scarlet fever showed negative skin reaction and 29 per cent had a positive reaction.

SUMMARY

There has been a downward trend in the mortality of certain streptococcic diseases. This is not true of puerperal septicemia, which is most commonly due to the streptococcus. We should not regard this with equanimity and feel that the minimum has been reached. Bacteriologic studies have been made and the virulence of organisms studied. Various antiseptic and aseptic technics have been applied. Many operative procedures have been recommended and tried. There still remains a residuum of infection sometimes fatal, often unaccountable. We cannot always avoid the possibility of accidental and unknown inoculation of the patient with streptococci and other pathogenic organisms. It is unavoidable that the genital tract be injured and its resistance to infection thereby lowered during parturition. Is it possible perhaps to determine in a measure the resistance of the patient to the more frequent and serious streptococcic infections and perhaps in some manner raise the resistance of those who are sensitive and presumably nonresistant to this type of infection? Certain individuals and races seem to have greater resistance to streptococcic infections than others. This is shown by a comparison of the mortality rates for the negro and the white from certain streptococcic diseases. The fatalities among negroes are greater than for the whites in puerperal sepsis and other puerperal causes. This may be due to poorer care, more complications, or possibly a varying susceptibility to different types of organisms. In a study of a series of cases it appears to be true that those who have had a previous infection with the streptococcus, as in scarlet fever,

are less liable to a morbid puerperium. It also seems to be indicated that a large percentage of those who die from puerperal septicemia do not seem to have had a history of scarlet fever and thus have had no opportunity to increase their resistance. So far as the skin test with streptococcic toxin is concerned, the majority of persons seems to be nonreacting, some of whom have had scarlet fever. Those who are not sensitive may be less prone to streptococcic infection.

CONCLUSIONS

1. In our attempts to curtail and if possible eliminate puerperal septicemia we should gain a clearer idea of the factors producing susceptibility and resistance to infection, especially with the streptococcus.

2. The relationship between streptococcic diseases and puerperal sepsis should be more clearly understood.

3. Natural and acquired immunity should be studied with reference to puerperal infection.

4. It is possible that the streptococcic toxin may afford us an index of the susceptibility of the patient to streptococcic infection.

5. It is also likely that one could build up the patient's immunity to streptococcic infection when this seems to be indicated in susceptible persons.

6. The relatively low incidence of scarlet fever and high rate of puerperal sepsis among the negroes could also be explained by the supposition that at an early age they were resistant to scarlet fever and that later in life they lost this relative immunity and had acquired no group immunity to streptococcic infections from having had scarlet fever and therefore were more susceptible to inoculation with the streptococcus.

7. As an incidental observation it might be noted that while the negro seems more resistant to certain known streptococcic diseases than the white, he seems to have about the same susceptibility to measles. This might suggest the possibility that measles is not a streptococcic disease.

N. B. We wish to acknowledge the helpful suggestions of Dr. W. P. Larson in the preparation of this material.

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LaSalle Building.

THE VAGINAL APPROACH FOR CERTAIN INTRA-PERITONEAL OPERATIONS*

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WITH a choice of several operative procedures a surgeon is prone to choose the method with which he is most familiar. Few operators are truly eclectic, most are guided by personal convenience, previous training and usage and often are unduly prejudiced by a single unfortunate experience.

The vaginal section has never been popularized despite the enthusiasts who have urged the advantage of the method. Especially through the nulliparous or atrophic vagina, access is difficult; vision is restricted and considerable experience desirable before any but the simplest type of drainage incision is made. To increase the exposure by a Schuchardt or Staude incision is only rarely warranted, and it is not surprising that the surgeon turns to an anterior abdominal section as a routine measure after having once experienced the difficulties of the vaginal route. Nevertheless, there are conditions in which the vaginal section gives a lower mortality and morbidity than an incision through the anterior abdominal wall and in which the access to the field of operation is more direct and at least not more difficult than by an anterior abdominal section. Therefore, it behooves every abdominal surgeon to study the method of approach to the peritoneum through the vagina and to acquire a degree of skill in this operation by training. Particularly for the obese patient with a relaxed or lacerated outlet does vaginal section commend itself for operations within the pelvis. Here it has the disadvantage of permitting but limited exploration of the abdominal structures above the pelvic brim. However, even delicate conservative operations upon the uterus, tubes or ovaries, the shortening of uterine ligaments, operations upon the rectum, pelvic colon, lower ureters and not infrequently the appendix and small intestine, may be carried out and often with greater facility than through a thick abdominal wall.

At this time it is not desired to consider the usual vaginoperitoneal operations for displacement, inflammatory disease or newgrowths of the uterus and adnexa but rather to indicate the occasional value of the vaginal approach in operating for affections of the peritoneum, intestine, appendix, lower ureters and base of the bladder.

For the operations requiring dependent drainage or the greatest possible exposure and for operations upon the rectum, intestine and

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appendix, the posterior colpotomy is to be preferred. For operations upon the base of the bladder, ureters, and for conservative operations upon the uterine ligaments and adnexa, an anterior colpotomy gives more direct access.

Peritoneal and Pelvic Infection.—The relatively greater resistance of the pelvic peritoneum to infection, the dependent drainage and the comparative immunity of the peritoneum, if irrigation is not used, from infection spreading upward from the external genital tract after a vaginal section, renders this route the preferred method of drainage for all acute infections that may be reached through the pelvis. Doubtless an important factor in the good results obtained is the very limited peritoneal irritation from exposure to the air, handling or other manipulation. Not only may many acute infections originating from the genital tract be handled best through the vagina, but certain infections involving or adjacent to the pelvis, originating in the appendix, rectum, colon or low-lying intestinal coils, may be treated with the lowest mortality this way. After perforation of the uterus, rectum or pelvic colon, the ureter or base of the bladder, an occlusion and drainage can be obtained through a vaginal section. Ureteral and intestinal openings drained through the vault of the vagina usually close spontaneously, at least if there is no obstruction below the opening. Where a low-lying intestinal coil has been severely damaged or partially separated from the mesentery, isolation of the injured area by iodoform gauze introduced through the vagina, although often followed by a vaginal intestinal fistula, is not infrequently succeeded by spontaneous closure in quite a surprising manner. As compared with the danger of general peritoneal infection from operations upon the lower intestine performed through the anterior abdominal wall, the vaginal route is relatively safe from infection.

Evacuation of Peritoneal Effusions.—Serum, blood or pus may be given exit from the peritoneal cavity by a posterior colpotomy and gauze drainage. For ascites a longer and more complete discharge of serum may be obtained than from an incision through the anterior abdominal wall. The drainage of the general abdominal cavity, however, is soon interrupted by the formation of adhesions. The vaginal incision is very useful for the removal of blood which often continues to come away for hours and days after the incision is made. The limited manipulation required is a great advantage where there is shock or collapse. In ectopic pregnancy or tubal abortion with much intraabdominal hemorrhage, the vaginal approach is often simple, rapid and relatively safe; all that is required being to pull down, clamp or ligate the affected tube and to introduce a large gauze drain into the culdesac. The operation may be completed in five or ten minutes and causes less shock than an anterior abdominal section. I have used this method in all tragic types of ectopic pregnancy for over twenty

years, the only death in the series being from a pulmonary complication three weeks after the operation. Normal pregnancies have occurred after this operation.

In certain cases of rupture of the lower segment of the uterus during labor, the uterine laceration may best be closed, the blood and possibly the placenta removed from the abdomen and drainage instituted through the vaginal opening.

Vaginal Enterostomy.—In an acute postoperative obstruction following celiotomy for pelvic disease the point of obstruction is usually within the pelvis. Often the operation has involved the separation of adhesions or the opening of septic foci. The condition may be due to a paresis of the traumatized bowel, to adhesions or to secondary gaseous distention producing a kink and obstruction. If the abdominal incision is reopened and the adhesions are separated, they will often reform with a continuance or recurrence of the ileus. At times repeated operations are done in the effort to relieve the patient. If, however, a vent is given to the distended intestine by a properly placed enterostomy, not only is temporary relief obtained, but an obstruction due to recent adhesions, pressure, or angulation of the intestine usually spontaneously disappears. Occasionally in such a form of obstruction, particularly where a bimanual examination shows the presence of distended intestine in the pelvis, a vaginal enterostomy gives immediate relief and is very efficient.

With the pelvis well elevated an incision is made through the posterior vaginal culdesac, the distended loop of gut exposed, isolated by gauze, a purse-string suture introduced, the enterostomy formed by a soft rubber tube of sufficient size around which the purse-string suture is securely tied. The tube is then brought out through the vagina and separated from adjacent structures by iodoform gauze packing. The operation affords drainage of the pelvis and is not complicated by the extrusion of intestine as often occurs when the anterior abdominal wall is incised. Not infrequently the incision also gives exit to septic or bloody fluid in the pelvis.

Carcinoma of the Rectum.—The Schuchardt unilateral or the Staude bilateral incisions are of great value in the complete removal of the rectum for carcinoma. Usually the operation forms the second stage after a previous suprapubic mobilization of the colon and a colostomy. The vaginal section enables the evacuation of the posterior part of the pelvis and the free excision of infiltrated vaginal or uterine tissue.

Ureter.—The lower end of the ureter is best exposed through an anterior or anterolateral vaginal colpotomy. With the posterior vaginal wall well retracted, the cervix is grasped by a vulsellum forceps and pulled toward the tip of the coccyx, the anterior vaginal wall divided transversely one centimeter anterior to the angle of reflexion of the bladder, the bladder demonstrated and carried forward

and the peritoneum opened. The edge of the peritoneal incision is fastened to the anterior edge of the vaginal incision by several interrupted sutures. The ureter is located in one of three ways as follows: (1) *By inspection.* Elevating the anterior margin of the incision the exposed fold of bladder is traced laterally where it is continuous with the ureter which passes into the adjacent parametrium. The ureter may then be brought down into the vagina by an appropriate blunt hook or nontraumatizing forceps. The ureter is recognized by the characteristic intermittent sliding or trombone peristaltic waves which are intensified by stroking the tube. (2) *By palpation.* The ureter, especially if thickened, dilated or containing a calculus or other foreign body, may be detected by the finger passed through the colpotomy wound. (3) *By ureteral catheter.* A ureter containing a sound or catheter may be readily located by palpation through the colpotomy wound.

Operations performed upon the ureter through the vagina include: (a) drainage for perforation or injury of the ureter; (b) ureterotomy for the removal of calculus or other foreign body; (c) the completion of a combined operation of ureterectomy for tuberculosis or other disease, the upper part of the ureter having previously been liberated by an incision of the abdominal wall; (d) the occlusion or implantation into the bladder of a supernumerary ureter causing a leakage of urine. (e) ureterovesical or ureterointestinal anastomosis. For the lateral anastomosis of the ureter to the bladder I have used a simple ligature method after the plan of McGraw's ligature method of gastroenterostomy, except that elastic traction was used instead of an elastic ligature. Contiguous portions of the ureter and bladder are transfixed by a fine curved needle carrying a strong linen or silk ligature which is then tightly tied to cause a pressure necrosis of the adjacent walls of the ureter and bladder and the formation of a new stoma. The ends of the ligature are carried through the bladder and urethra by the aid of a small probe and traction applied by means of a small rubber band fastened by adhesive plaster to the thigh. The urethra is protected from pressure by threading the ligature through a section of rubber catheter. Under the slight but continuous traction the ligature comes away in five to seven days leaving an ample opening into the bladder. The peritoneum should be guarded for forty-eight hours by a small drain of iodoform gauze, although little leakage of urine through the vagina may be expected. (f) The ureter or ureters may be implanted into the sigmoid or pelvic colon by the vaginal route in patients with a fairly capacious vagina. The method of Madl, Peters or Coffey may be used, the loop of bowel being pulled well into the vagina to give convenient access.

In fractures of the pelvis with rupture of the base of the bladder suture and drainage are, at times, feasible through the vagina with a

minimum of shock. Occasionally a portion of the base of the bladder may be resected or otherwise treated for newgrowth or diverticulum through the anterior vaginal wall.

Appendicitis.—In acute appendicitis there are three great dangers: first, the patient's friends who feed and purge the victim; second, the attending physician who delays and does not enforce complete physical and intestinal rest; and third, and not the least, the overactive surgeon. Robert Morris has particularly emphasized the danger of unnecessary and prolonged operations in the presence of peritoneal infection. During the second stage of peritonitis from appendicitis, it is the exposure and damage to peritoneal surfaces during operation which is to be especially feared. By free exposure, by introducing the hands into the abdomen, by manipulation, evisceration, sponging, irrigation, unnecessary suturing, the peritoneum is converted from a protective to an absorbing membrane, and the mortality of diffuse peritonitis from appendicitis rises from 7 to even 85 per cent. For the surgeon so constituted that he cannot withhold his hand in operating for septic forms of appendicitis the vaginal route with its lack of access would be a large protective factor for the patient. Of course no one would advocate vaginal appendectomy as a routine procedure, yet a diffuse purulent peritonitis may be drained and low-lying purulent collection of appendiceal origin may be evacuated by a posterior colpotomy. I have removed the appendix or drained appendiceal abscesses through the vagina about fifteen times, a small proportion of the total number treated. In a number a quiescent appendix was removed through the posterior culdesac in association with other pelvic operations. From this small experience, without mortality, my impression is that when feasible the vaginal route is a relatively safe approach.

With a patient in high Trendelenberg position the appendix is not infrequently seen as the trowels are moved to inspect the various portions of the pelvic cavity. The appendix is pulled down by a sponge forceps, the base doubly ligated and divided, and the mesoappendix tied with the same ligature over the stump. A gauze drain is left through the vaginal opening.

A plea is made for greater familiarity with the forms of colpotomy that the abdominal surgeon may make use of this valuable procedure in the occasional condition for which it is indicated.

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FACTORS GOVERNING BLOOD LOSS IN THE THIRD STAGE OF LABOR

(A Preliminary Report)*

By L. A. Calkins, M.D., Ph.D., University, Va.

ONE OF the many unexplained facts in obstetrics is the marked variability in the loss of blood in the third stage of labor. Obviously more definite knowledge of the factors underlying this variation is highly desirable. The present study, of which this paper is merely a preliminary report, contemplates the determination of some of these factors and the laws governing their operation. There were available for this study 868 consecutive deliveries past the thirtieth week. Fifteen of these patients were delivered by cesarean section, leaving 853 cases delivered vaginally and hence suitable for this investigation. The average blood loss in this group of 853 cases was 222 c.c. This average compares very favorably with others published in the literature. DeLee and Hirst each estimate an average of 250 c.c. Williams computed the average of 1000 cases and found it to be 344 c.c. Ahlfeld's average on 2058 cases was 505 c.c. Other averages include those of Champneys (300 c.c.), Tucker (300 c.c.), Commandeur (500 c.c. to 600 c.c.), and Tarnier and Chantreuil (600 c.c. to 700 c.c.).

Not only do the several averages show a considerable variation, but the range of the individual series is also quite variable. Our cases ranged from zero to 1500 c.c. Williams' 1000 cases ranged from zero to 2400 c.c. Ahlfeld reported one case with a loss of 3250 c.c. followed by recovery. This element of variability is so great that we have not had, in the past, a satisfactory definition of what should be regarded as normal loss and what should be looked upon as pathologic. An arbitrary limit of normal has been set by three different writers. DeLee and Hirst place this limit at 500 c.c.; Williams at 600 c.c. Eighty-seven per cent of Williams' cases were under 600 c.c. As far as our series is concerned 600 c.c. would seem to be about the proper limit of normal. Ninety-six per cent of our cases lost less than 600 c.c.

Our technic of measurement of the blood loss is as follows: At the first show of blood, after delivery of the child, a sterile hand basin is placed against the perineum between the vulva and anus. The placenta and associated blood are caught in this basin. The basin is held in place until the active bleeding has been controlled. The blood in the pan is then measured in a graduate and is labeled the measured loss. In the majority of cases there is other bleeding previous to the placental stage, either from laceration or episiotomy, or subsequent to it from imperfect contraction of the uterus, injuries to the birth canal, etc. This amount

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is estimated, care being taken not to underestimate it. This second portion is called the estimated loss. While theoretically the method employed in arriving at this latter amount is subject to error it is believed to be accurate to 25 c.c. on the average. It was selected in preference to the more accurate method of Williams because of the desire to separate the placental stage blood from other bleeding, as different factors might be involved in the two types. The sum of the measured loss and the estimated loss equals the total loss. Analyis of each of the three values has been made. Williams' method is as follows: "Immediately after the birth of the child a sterile douche pan is placed under the buttocks of the patient where it remains until all bleeding following the birth of the placenta has ceased. The entire amount is then poured into the graduate, accurately measured in cubic centimeters and noted in the history."

Certain types of cases in the series of 853 were found unsuitable for inclusion in an analysis of normal labors (Table I).

TABLE I

	CASES	AVERAGE C.C.
Placenta previa	22	351
Hydramnios, myoma uteri, retained placenta, etc.	5	410
Median (and high) forceps	12	428
Third degree lacerations	3	358

Excluding this group of abnormalities there were 809 cases remaining for analysis (average blood loss 213 c.c.). Of these 533 were white women with an average blood loss of 223 c.c., and 276 were colored women with an average loss of 198 c.c.

Certain other types of abnormalities and complications were included in the analysis because the average blood losses were not materially different from the general average (Table II).

TABLE II

	CASES	AVERAGE C.C.
Slightly More Than Average Blood Loss		
Toxemia of pregnancy	61	261
Deformed pelvis	23	245
Low forceps	53	292
Version, combined podalic	17	232
Breech presentation	31	233
Slightly Less Than Average Blood Loss		
Twin pregnancy	9	203
Syphilis	41	193
Anemia, severe	10	170
Bag, Voorhees'	17	185

Analysis of the 809 cases, including those in Table II, was first made. It was further noted, however, that the type of laceration received has some effect upon blood loss.

First degree laceration	273 cases	199 c.c. average
Second degree laceration	116 cases	240 c.c. average
Episiotomy	72 cases	272 c.c. average

Wishing to eliminate all possibility of the effect of abnormality on the coefficients, a second set of analyses was made on the 516 strictly normal cases. (By strictly normal we mean not more than first degree laceration, no complication, and no operative procedure.) The average blood loss in this group of 516 normal cases was 207 c.c.

Further refinement by classes or groups was not possible because of the small size of the present series, although it was noted that:

Private cases had an average blood loss of 235 c.c.
White ward cases had an average blood loss of 225 c.c.
Colored ward cases had an average blood loss of 200 c.c.

Moreover the work of the interne is not negligible. Fourteen consecutive internes, each serving three months, showed:

In the first month an average loss of 238 c.c.
In the second month an average loss of 223 c.c.
In the third month an average loss of 211 c.c.

This was in spite of the fact that the resident or a visiting man was present at each delivery.

Pearson's coefficient of correlation has, so far, been used exclusively in these analyses.*

The results of the first series of correlations (on the whole group of 809 cases) are listed in Table III.

TABLE III. CORRELATIONS (ALL CASES)

Age of mother	−0.007 ±0.024
Parity	−0.056 ±0.024
Length of gestation	+0.140 ±0.029
Conjugata vera	+0.062 ±0.026
First stage of labor	+0.067 ±0.025
Second stage of labor	+0.127 ±0.024
Third stage of labor	+0.118 ±0.024
Height of mother	+0.119 ±0.029
Weight of mother	+0.162 ±0.030
Length of baby	+0.180 ±0.025

From Table III one might draw the following deductions:

1. The age of the mother has no effect on the blood loss.

2. Parity probably has no effect, as the coefficient, besides being small, is hardly more than twice its probable error.

*Coefficient of correlation $(r) = \frac{\Sigma xy}{N\sigma x\sigma y}$ where x, y are deviants from the mean of X, Y; N is the number of cases, and $\sigma x \sigma y$ are the standard deviations of the means of X, Y. This coefficient is very satisfactory because of its applicability to partially correlated biologic phenomena. When the two variables are perfectly proportional to each other, the coefficient is plus 1.0; when they bear no relation, one to another, the coefficient is 0.0; and when they are in perfect inverse proportion to one another, the coefficient is minus 1.0. Any value between zero and plus 1.0 indicates a direct proportion correlation, and any value between zero and minus 1.0 indicates an inverse proportion correlation. It is very rare in biologic phenomena to find correlations greater than plus 0.5 or minus 0.5.

3. Length of gestation beyond the thirtieth week has a definite though small effect, as the coefficient is more than four times its probable error. This coefficient is, however, smaller than that for the length of the baby, and so the effect of the length of gestation is to be explained on the basis of a coexistent increase in height of the child.

4. The size of the pelvis has but little if any effect on the blood loss. The coefficient is only slightly more than twice its probable error. The same seems to be true of the length of the first stage of labor.

5. The length of the second and third stages of labor would seem to have some effect on the blood loss, as their coefficients are more than four times the probable errors. The same might be said of the height of the mother.

6. The weight of the mother shows a larger coefficient, more than five times its probable error, and shows a definite effect in direct proportion on the blood loss.

7. The size of the child seems to be the most important factor of this group, affecting the blood loss in direct proportion.

When we come to the consideration of the coefficients for the series of 516 normal cases we find in Table IV:

TABLE IV. CORRELATIONS (NORMAL CASES ONLY)

First stage of labor	+0.101 ±0.032
Second stage of labor	+0.060 ±0.032
Third stage of labor	+0.070 ±0.032
Height of mother	+0.109 ±0.037
Weight of mother	+0.130 ±0.040
Length of baby	+0.139 ±0.032

1. The length of the first stage of labor appears of more importance than that of the second or third stage but none of them are particularly significant.

2. The height and the weight of the mother still show coefficients of about the same magnitude, but because of the small size of this series their probable errors are larger, and their significance must remain somewhat in doubt until a larger series can be analyzed.

3. The length of the baby has a coefficient which is more than four times its probable error. This coefficient must, therefore, be regarded as significant.

Determination of the coefficients for the component parts of the total blood loss shows a rather significant result in Table V.

Very evidently the measured loss is the part affected both by the size of the baby and weight of the mother.

None of the above factors show a marked effect on the blood loss. Several of them seem to have a small effect. Analysis of a series of at least 4000 cases will reduce the probable errors to such a point that more definite conclusions can be drawn. Further search for other fac-

tors such as the size and weight of the placenta, blood volume of the mother, coagulation elements of the mother's blood, and blood pressure, must be made.

TABLE V. CORRELATIONS (NORMAL CASES ONLY)

Total blood: Length of baby	+0.139 ±0.032
Measured blood: Length of baby	+0.175 ±0.133
Estimated blood: Length of baby	+0.075 ±0.134
Total blood: Weight of mother	+0.130 ±0.040
Measured blood: Weight of mother	+0.144 ±0.040
Estimated blood: Weight of mother	+0.001 ±0.042

If definite knowledge of the physiology of blood loss can be acquired, it may be possible to determine the etiology and nature of the excessive bleeding in the various types of cases where hemorrhage so frequently occurs.

At this point in the study the following conclusions seem justified:

1. Pearson's coefficient of correlation affords an excellent medium for this type of investigation.

2. Age of the mother has no effect on the blood loss at delivery. Parity has little or no effect.

3. There is a direct proportion between the length of the baby and the blood loss (most marked in the measured loss). This effect is definite but not large.

4. The height and weight of the mother probably affect the blood loss in direct proportion.

5. No one of the factors studied exerts a major effect on the blood loss. Further decrease in this amount must, therefore, come through improved management of the third stage.

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THE TEACHING OF OPERATIVE OBSTETRICS*

By A. M. Mendenhall, M.D., Indianapolis, Ind.

During the last few years the writer has been greatly interested in the number and variety of articles in the literature on obstetric mortality and morbidity. Comparatively few journals on obstetrics or on medicine in general are being published which do not contain someone's view as to the cause of our glaring failures.

Articles on needless obstetric operations, improperly chosen operations, unskillfully performed operations, poor training in obstetrics, high maternal and fetal death rate, etc., are appearing regularly and frequently.

A very careful collection and study of these essays reveal a great deal of destructive and but little constructive criticism. They give us a carefully developed diagnosis with but little or no suggestions as to treatment. We all must admit there are many causes contributing to our very undesirable rank among civilized nations in our obstetric results. We all admit that the remedy is not to be found in the solution of any one problem. There can be no doubt that the midwife as she exists in America is a menace. Very few of our schools have given obstetrics a proper rating in the curriculum. Many schools are poorly equipped to teach obstetrics. The laity is poorly informed as to the importance of child bearing. It is possible that some of our high ranking obstetricians are teaching major obstetric surgery in a way that misleads and misguides the poorly trained obstetric attendant.

The writer is ready to admit that all these factors and many others have a bearing upon the very unsatisfactory progress but wishes to direct attention especially to our present way of teaching operative obstetrics and to suggest some changes.

Many authorities have shown that approximately 35 per cent of the young doctor's practice is obstetrics, whereas only about 4 per cent of the four years' course in medicine is allotted to the obstetric department.

On the other hand surgery which will be represented by about 5 to 10 per cent of the recent graduate's time, is given 18 per cent (exclusive of the surgical specialties) of the teaching hours. We all realize furthermore that almost all the general surgery coming to the young physician is minor in type.

Yet this same young physician is presumed to be competent to do at least all ordinary obstetric operations.

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The Committee on Maternal Welfare has repeatedly given us all these figures and has demanded a remedy.

Many authorities, among them Polak, Newell, E. P. Davis, Lynch, Rowland, and others have insisted that the general practitioners are doing too much obstetric surgery.

The Committee on Maternal Welfare says: "It is not expected that the general practitioner shall do cesareans and other obstetric operations," but the writer maintains that he *is* doing far too much operative obstetrics. The young doctor may not often be doing cesareans, but he is quite generally doing forceps deliveries, internal podalic versions, craniotomies, episiotomies, third degree repairs, and in fact ordinary perineorrhaphies, and has only an inadequate training.

A few years ago the writer investigated the obstetric departments of a number of our leading schools and found that most of the teachers admitted that comparatively few of their students ever assisted at a forceps delivery.[1]

Is our teaching correct in this respect? Is it right that we should deliver a few high sounding lectures on the history and development of the obstetric forceps and describe and display the various types of instruments and their different locks and parts? Is it right that we should didactically orate on the indications and contraindications and manner of applications without these well-delivered lectures being supplemented by opportunities for the student to develop his ability to use an instrument which is fraught with so much danger?

There will be some who suggest the manikin. We accept the manikin as a very great addition to our teaching armamentarium, but it falls far short of a demonstration on the living patient.

A great deal can and must be taught by individual instruction in the many obstetric procedures on the manikin, but this is only an introduction and should be used to lead up to the same operations upon the living patient.

There is a very important place in our curriculum for manikin demonstration, and in many schools it is being used very advantageously, but it can never be a substitute for the woman in labor.

Teaching operative obstetrics from the lecturer's platform is apt to leave the student under the impression that obstetric surgery is simple and easy.

At least we are confronted with the fact that the average neophyte in medicine has little hesitancy in attempting any ordinary obstetric operation without assistance and often in the patient's home, using any available woman or other layman as an anesthetist.

Are we properly dignifying obstetric surgery? We have all had much to say in recent years about obtaining proper recognition for the general subject of obstetrics. Most of us feel that there should be three and only three major departments in our medical schools—*medi-*

cine, obstetrics, surgery. We have advocated this in many ways and have sometimes gained ground, although just now there seem to be some obstacles to progress.

It must be admitted that before we can hope to give a thorough practical course in operative obstetrics to undergraduate students, we must have much more time allotted to us in the curriculum and much more and better clinical facilities than the average school possesses.

We cannot overlook the fact that at present we have none too many hours to teach the physiology of so-called normal pregnancy, labor, and the puerperium.

Our students must be thoroughly drilled in obstetric physiology. They must be carefully taught to distinguish between the normal and the pathologic. They must be instructed in detail as to the value and importance of prenatal care. They must be taught the fundamentals of obstetric pathology and how to recognize and treat the many deviations from normal physiology. And all this requires time. In fact it requires so much of our present number of hours that we have not the time left for a proper teaching of obstetric operations.

Furthermore, very few clinics approach in size the number of cases necesary to teach operative obstetrics to the average sized class. The teaching capacity of an obstetric patient is greatly limited. Not more than one or two students can secure any valuable instruction in an obstetric operation on one patient. Obstetric operations can rarely be scheduled. The student is not always available at the proper time. For these and other reasons it requires a very large number of obstetric patients to secure adequate teaching in obstetric surgery to an average class of students.

A clinical amphitheater is a help, but merely observing obstetric surgery is not enough.

A combination of obstetrics and gynecology under one head makes for better teaching of both subjects. Obstetrics in its modern and broader sense should include all obstetric operations and pelvic surgery. All else should go to the department of general surgery. Normal obstetrics, obstetric operations and pelvic surgery are inseparable. No one can be considered competent in gynecology who is not thoroughly trained in obstetrics, nor is one properly trained in obstetrics who has not the ability to handle all obstetric operations.

Hence from a pedagogical standpoint we should not recognize any independent department of gynecology.

There has been marked progress in the last two decades classifying surgeons. The laity now rather generally demands that some one other than the general practitioner shall be called upon for surgery. The College of Surgeons and other influences have done great good in attempting to ascertain who is competent to do major surgery. A very large part of obstetrics is surgery, and surgery of the greatest impor-

tance. The obstetric surgeon is practically always entrusted with the lives of two patients rather than one.

Shall he be permitted to stumble ahead in this important field with little or no training? Will we continue to permit the laity as well as the young graduate to believe that he is not quite equal to an appendectomy but is able to assume immediate and sole responsibility for major obstetric surgery? Whether the question is answered yes or no, the fact remains that just such a condition exists at this moment, and there seems to be some apathy about finding a remedy.

A recent writer attempts to explain our high fetal and maternal mortality by suggesting two causes.[8] "Ignorance on the part of the public of the dangers connected with childbirth and the need of skilled care and proper hygiene to prevent them, and the difficulty of securing proper obstetric care—and that the public still regards childbirth as an entirely normal process. This has reacted on the medical profession, producing low fees, so that, with the exception of the city specialist, obstetrics has become the worst paid, although most difficult and exacting branch of medicine."

Newell recently gave us food for much thought when he reported the astounding obstetric mortality in Massachusetts and showed that a large part of it was the result of needless obstetric surgery and the attempt of poorly trained operators to do major obstetric surgery.

The average practitioner is not competent to handle a severe case of postpartum hemorrhage, placenta previa, prolapsed cord, abruptio, or contracted pelvis. He may be and often is able to make a fairly accurate obstetric diagnosis and probably could write a good outline for treatment but will frequently be quite incompetent to carry out the proper obstetric operation.

At present the teaching in surgery and gynecology is mainly to develop the student's ability in diagnosis, while little effort is made to teach operative precedures, since it is not presumed that the new graduate will go out and do major surgery before he takes special training. Only last year our retiring president admitted that our graduates are not properly equipped to do obstetric surgery.

Dr. Polak[2] says the average graduate is a "fair midwife, nothing more."

Holmes[3] says, "The fact that the death rate among emergency cases (that is, those sent in by medical attendants) is over 10 times that of regular applicants in the New York Lying-In Hospital is a reflection on the preliminary medical training of the profession." He further states that the proper place for the study of obstetric surgery is in postgraduate courses intended for those preparing for the specialty. But this latter statement overlooks the fact that a very large number of women are still being delivered by the general practitioner and not

by those specially trained in obstetrics, and that there are comparatively few places where advanced obstetrics can be studied.

The writer in a former paper[4] advocated more specialists in obstetrics. It would be a distinct advantage if more trained obstetricians were available at least as consultants. We realize it is a great misfortune when the family doctor in need of a consultant is compelled to call a general surgeon. Except for cesarean section alone, the general surgeon is rarely any better obstetrician than the family doctor and usually falls far short of the ability to ascertain the indications and contraindications even for cesarean section. If more trained obstetricians were properly distributed over the country and if the laity and medical profession were cognizant of their ability and availability, they would supply a very definite deficiency and fewer needless and unsuccessful obstetric operations would be performed.

But what are the opportunities for such training? The number of positions available to men who wish to make a special study of obstetrics are still very few. In 1921 it was shown that many men were clamoring for such opportunities,[5] and the condition has been but little bettered since.

In Sweden a six months' residency in obstetrics is required.

E. P. Davis says, "Of the medical profession the general practitioner is the greatest danger in obstetrics," and that "He must do obstetrics to keep the family and he must do obstetric surgery because his colleagues do."

Stoeckel[6] reports 55 cases where obstetric operations were instituted in the home and failed. Thirty-nine of these were high forceps and no indication in 37. Twenty-seven babies died; 4 mothers died.

In London the Committee from the Royal Society of Medicine states that "The general practitioner tends to regard himself as an obstetric specialist and feels that to call in a specialist is a confession of weakness or failure." They further state that "meddling through is a prevalent practice and it is legitimate to trace it in some measure to training in practical midwifery." This would seem to indicate that conditions are no better in London than in America.

A recent American writer[7] says that 10 per cent of our obstetric deaths are the direct result of operations.

Some will say that obstetric surgery must be taught during the intern year. Possibly this is correct, but we meet with at least two difficulties. First, there are a few graduates still who go into practice with little or no internship. Second, a very large number of our so-called acceptable hospitals have but few obstetric cases, and many times these are private cases or are handled by men not trained in obstetrics so that the obstetric service would be of little or no real value to the intern.

Would it be Utopian to hope that obstetrics will attain recognition in the not too distant future when our acceptable hospitals will give a satisfactory service in obstetrics?

But too many of these solutions for the problem are looking far into the future.

The present situation confronts us as follows:

1. Our students are graduating with little worth-while training in obstetric surgery.

2. They are graduating with the feeling that they are able to do obstetric surgery.

3. The laity still believes that the young doctor as well as the old family physician is equipped to do major obstetrics.

4. At present our hospitals are not giving and cannot give satisfactory training to their interns in obstetrics.

5. Not enough trained obstetricians exist in many locations to supply the demand as obstetric consultants.

6. Opportunities for postgraduate study in obstetrics are still not sufficient to supply the demand.

7. The teaching of operative obstetrics in the average school at present is quite unsatisfactory and may often misguide and mislead the student as to the importance of a thorough training in obstetric surgery.

8. Before we can properly teach operative obstetrics, we need more hours in the curriculum, good clinical amphitheaters and much larger obstetric clinics.

9. Shall we continue this unsatisfactory training, or shall we avoid all attempt at teaching major obstetric surgery to the undergraduate and compel him to obtaining this training later?

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PROBLEMS ASSOCIATED WITH THE CERVIX*

By R. R. Huggins, M.D., Pittsburgh, Pa.

ONE of the most gratifying things in medicine is the wonderful progress made during the last twenty-five years in the prevention of disease and reduction in mortality. It is rather remarkable that while there has been a satisfactory reduction in the mortality of tuberculosis, there has been a corresponding increase in cancer and little change in puerperal sepsis or the frequency of injuries to the cervix and pelvic floor. The reduction in the mortality of tuberculosis and many other diseases has not been due altogether to the discovery of the active cause of these diseases but to a more intelligent appreciation by both the public and the profession of the underlying influences. For the reason that no definite cause has been assigned to cancer and, because of its frightful mortality, we have been slow, as a profession, in asking the public to share with us the responsibility of more active measures in its prevention.

The physician's office will soon be filled with people who come to consult him with reference to the state of their health rather than wait until sick. They already desire to find out if they are up to their own normal and if their resistance is such that they will be able to withstand the invasion of infecting organisms and the strain incident to the stress of life. In other words, we have entered the period of prevention and it marks a new era in the progress of scientific medicine. It would seem that it is the duty of the members of this organization to teach more actively both the public and the profession that which they know about prevention rather than continue to stress the symptoms of the later stages and the technic of operative measures which often fail either in relief or the saving of life.

For these reasons, the problems of the cervix, as above indicated, should be considered from this standpoint. One is inclined to wonder whether the inaccessibility of the cervix, and its minor and somewhat subservient position to that of the uterus, has not led to a lack of a keen appreciation of some of its problems. When we consider the great amount of inconvenience, suffering and misery, and, finally, death, that grows out of various kinds of disturbances which have their origin in this small area, it would seem that while much has been said and written, there still remains a responsibility among those who are teachers and leaders in gynecologic and obstetric work. It holds an interesting study from the standpoint of anatomy. Here within the

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short space of one inch are four different kinds of epithelium. Beginning with the squamous cells covering the vaginal portion we find immediately adjacent within the canal a mucous membrane composed of complicated racemose glands, lined by cells of the high cylindric goblet cell type. We have not learned, as yet, whether there may not be other important functions in these glands except the simple supply of a mucus secretion. As the internal os is approached, this mucous membrane becomes modified and we find the glands becoming less arborescent and the high cylindric epithelium lower in type. At the internal os, the simple tubular glands with a low cuboidal epithelium are found. The surface of the epithelium of the canal differs little with the exception that it is ciliated. The glands from the cervix produce a mucus secretion but in the endometrium there is only a thin secretion which is not true mucus. There is a difference both in their histologic structure and physiologic function. The manner in which infection may differ in its effect upon these two kinds of cells, so immediately adjacent, at once incorporated the aid of the bacteriologist. One is reminded of the problem of Europe, small countries of different kinds, so closely situated.

As long as the mucous membrane of the cervical canal remains unbroken, either by instrumentation or parturition, it seems to act as an efficient barrier to all organisms except the gonococcus, tubercle bacillus, and the spermatozoon. The chemist is not free from responsibility for here we have an acid secretion in the vagina and immediately adjacent within the canal an alkaline one. The constant bathing of cells which were intended to remain in an alkaline solution with acid as occurs in so-called erosion of the cervix may be of greater significance than we now know. With even the minor injuries which always necessarily accompany parturition, it is not difficult to understand the displacement of the various epithelial elements or so-called metaplasia. It may be of the utmost importance as to how these misplaced cells behave in their altered environment.

With reference to leucorrhea, it is conceded by all that one of its most important sources lies in the infection harbored within the mucous membrane of the cervical canal. Careful study of the anatomy of the cervix and a keen realization as to what happens to it, both in labor and in gonorrhea, makes it easy to understand its pathology. We are all familiar with the appearance of the cervix immediately after delivery. Bruised throughout and lacerated in hundreds of places, with exposure of blood vessels and lymphatics, the wonder of it all is that results are not worse. It is now generally believed that many cases of puerperal infection are caused by bacteria which have been harbored and protected previous to delivery in the tiny spaces provided by the complicated glandular arrangement in the cervical

mucous membrane, which has been crippled and deprived of its usual resistance by previous infection. While subinvolution, which is often followed by chronic deep-seated changes in the musculature of the uterus, may be due to infection from within the uterine cavity, much of it comes from infection which is harbored in the cervix and which might be prevented if proper attention were given to the healing of these injuries after delivery. Students and practitioners of obstetrics should be taught that their responsibility does not cease on the tenth day after delivery. Every case should be followed until the cervix is thoroughly healed and involution complete. No woman should be discharged until the cervix presents a normal appearance and it might well be added until the normal relationship of the muscles and fascia of the perineum have been restored. The same holds true in the treatment of a cervix after the acute stage of gonorrhea. Dickinson has called our attention to the carelessness of the gynecologist in his responsibility to infection within the cervix. Both the obstetrician and gynecologist have been so busily engaged in originating and perfecting major operative procedures that they have not given proper attention to the lesser and more important phases, which, if properly carried out, might do away with the necessity for many operations.

The specialist in genitourinary disease refuses to acknowledge the title venereologist. The gynecologist, with equal fervor, is entirely too much engrossed with the bigger problems to give sufficient time and attention to the proper care of the subacute neisserian infection. We need men in general practice, well trained in obstetrics and gynecology, who will do routine work in these fields.

In addition to the necessity for a keen realization of the changes which are secondary to a low grade infection within the cervix, it is important that in our teaching we make it clear as to what the pathologic changes of a chronic cervicitis, with so-called erosion, really are. Williams, at the last meeting of the American Gynecological Association, stated that in a series of cases where there was elevation of temperature postpartum, 40 per cent had not been examined. The impression must be that the infection is carried at some point and the best probable location must be the cervix. He also stated that there were twice as many infections among the black women as in the white and concluded that this may account for the relatively high mortality in this country as compared to others not inhabited by the colored race.

The proper conception of so simple a process as erosion of the cervix makes it much easier for the student to understand how it can give rise to so many serious complications. The bright red velvety patch surrounding the os, as seen through the speculum, has been termed an erosion. This is a misnomer. It is not an ulcerative and neither is it a granulative surface. The vaginal portion of the cervix in this instance becomes covered by a single layer of columnar epithelium which

has grown downward from within the cervical canal. Its red appearance is due to the thin covering of these columnar cells. In the healing process the layer of columnar cells, with its intricate glandular system, often becomes covered over by the extension upward of the squamous cells which cover over the vaginal portion of the cervix. In this way small cysts form. This pathologic process, or so-called erosion, begins either after childbirth, where there are numerous tears, or after infection. Care should be taken that the student thoroughly understands the pathology of this condition, for, while it seems trivial, it is most important. A clear understanding leads to a much better appreciation of the relationship to extension of infection and also cancer of the cervix. Unless special care is taken to make students learn this change in detail they will pass over it and fail to get this most important link. They will acquire a good knowledge of cancer of the cervix but this seemingly unimportant change, which may bear a very important relation from an etiologic standpoint, will be entirely overlooked. It should be remembered that after a certain time has elapsed superficial and comparatively simple changes may lead to an extension of infection throughout the cervix and the uterus as well.

When we stop to consider that little more than sixty years have passed since the origin of cancerous growths has really been understood, we should not become discouraged with the progress already made. During this comparatively short time, the literature on carcinoma of the uterus has increased tremendously, and there is little doubt that while we may not within the near future discover the exciting cause, yet we are rapidly acquiring certain knowledge which if applied in a practical way will go far toward reducing the rapid and widespreading tendency to the increase of this disease.

At the present, there is only one known way to combat cancer mortality and that is by the recognition of the process in its earliest stages or better to identify those lesions which are definitely known to be the forerunner of malignancy. Proper understanding and the recognition and correction of some of these early changes may greatly reduce the mortality of cervical cancer. When the fact that one woman out of every twenty-seven will die of cancer of the uterus secures a serious hold upon our minds then any method or theory which may diminish this possibility will receive attention. There are certain outstanding factors which are quite apparent in a discussion of the predisposing causes in cancer of the cervix. It is well known that women who have never borne children, or where there has never been any previous inflammatory process within the cervix, rarely develop malignant change of that organ. While it remains within the province of the bacteriologist or chemist to finally solve the actual process in cancer, there are certain outstanding basic principles in its growth and development which are appreciated by the clinician and

he should assist in the cultivation of this field which at present may be designated as "No Man's Land." There is undoubtedly a stage in the development of this disease which lies between its earliest inception and the condition in which it may finally be demonstrated as a true malignant change. There must be a period of time unknown at present where there is an ending of certain disturbed cell changes, which are not known as malignant ones, and the beginning of definite malignant change. Clinical experience has clearly demonstrated that there is a time when a growth from its macroscopic appearance suggests malignancy and yet when examined under the microscope shows changes which are not definitely malignant. This is now referred to as the precancerous stage. Ewing says, "It is not true that a pathologic condition must be either cancer or not cancer. It may be neither the one nor the other. Before an appreciable amount of invasive features can be found all kinds of variations may be present in the type of cell and amount of proliferation." It requires little imagination under these circumstances to picture a malignant growth in the developing stage. It is interesting to note that such changes nearly always occur in the presence of chronic inflammation. While the gulf between the cells of normal tissue and the cells of malignant tumors remains hidden and unexplained, the absence of any explanation should not blind us to the existence of certain clinical facts that are of great importance in a very practical way.

Virchow was an earnest believer in the theory that irritation was an important factor in the etiology of cancer. It remained for Fibiger to produce carcinoma in the stomach and esophagus of rats by infecting them with spiroptera, the cause of the malignant change being irritation of the mucous membrane by the parasite. Repeated applications of coal tar to the ear of rabbits has led to the conclusion that continuation of chronic irritation may cause a precancerous condition in epithelium previously normal. It is evident that the study must begin in the individual cell and it seems probable that the predisposing cause is a chemical one because tissue does not react the same to all forms of irritants. The constant bathing of an erosion of the cervix with its accompanying inflammation in a purulent acid secretion must be an important factor in the cause of malignancy. The period of time over which this may occur before cancer ensues is especially important and should be given due consideration. While we do not yet know the exact cause for this peculiar change, we know that for some reason the growth we call cancer is a proliferation of cells previously normal which increase in number until a mass is formed which attracts attention as a result of the changed condition of the normal structures. This does not happen in a day or a month and clinical experience teaches that it is a slow growth with its origin, perhaps, in a single cell which has renounced its allegiance to the normal body control.

How long the cause may have existed before the onset of malignancy is unknown. It is probably true that we can seldom anticipate when cells may rebel and a mutiny ensue, but if on the alert we can keep all points subject to local irritation and infection free from chronic inflammatory change and by this means prevent the end-result, which, in some instances, is undoubtedly cancer. It is important to bear in mind that the chemical reaction within the uterus is alkaline, in the vagina, acid. The vaginal canal must necessarily contain a great number of various kinds of microorganisms. The inside of the uterus, under normal conditions, is sterile. When the cervix sustains tears which evert the cervical mucous membrane into the vaginal canal, it is quite probable that conditions are favorable to the development of malignancy. The cells of the cervix which ordinarily live in a field which is alkaline and sterile are thrown into a field where the reaction is acid and where there is infection. We do not yet know the reaction of cells under these changed conditions. Infection, under these circumstances, ascends into the cervix and body of the uterus producing a mucopurulent discharge which pours over the injured cervix, thereby causing further irritation. The epithelium from the vaginal and uterine sites both grow in and fill the defect with the result that the squamous cells become displaced deep into the cervix sometimes filling the glands and sometimes covering the gland cells.

It not infrequently happens that pathologists report suspicious changes in specimens of amputated cervices which suggest the possibility of malignancy. Displaced epithelium as a result of previous injuries and chronic inflammatory changes is quite common here and some of these so-called precancerous changes differ so little from what later is undoubted cancer that their importance cannot be overlooked. We look upon some of these cases, where the signs have been so characteristic, as potentially malignant and the operation of amputation of the cervix as having been a truly preventive one so far as cancer is concerned.

In 1906, I presented a paper under the title of "Pre-cancerous Lesions of the Cervix," in which four cases of cancer of the cervix were reported which had been under my care and observation for a considerable period previous to any evident development of malignant change. These patients all had been treated for cervicitis and carefully observed for two or three years previous to the development of any of the active symptoms of cancer. The development of malignancy which seemed to have been literally grafted upon these diseased cervices made a deep and lasting impression and has led to a firm conviction that there must be some association between these conditions. Since that time, we have continued to stress the importance of this relationship in our teaching. The observation from time to time of certain close relationships, between what may be benign and malig-

nant changes, led to the more firm opinion that nothing is yet known about the life of cancer. In other words, it is yet to be discovered how long a given cell may be in a state of irritation and undergoing certain mild changes before it finally assumes its true malignant form. It is here that close cooperation must be carried out by the clinician and the pathologist, neither of whom should be guided by preconceived ideas or prejudices in the study of cervices undergoing these chronic inflammatory processes. It is important that the pathologist has a keener interest in the history of these patients and that he sees the cervix in situ, so that he can acquire a better appreciation of the appearance of the cervix and its environment. This, together with a careful section over many areas, after its removal, may finally lead to a better understanding of what the true precancerous stage may be, or at least definite knowledge of the intervening cell changes.

Hunner has given to us a method of treatment for erosions and other chronic infections within the cervix, which, as a preventive and curative measure, should place his name in the Hall of Fame. Cauterization of the cervix, if properly used, will save many lives and give comfort to a greater percentage of women than any other simple procedure in surgery. It should be emphasized, however, that it is an operation which must be used effectively or its results will be disappointing. This is true in the more chronic and deep-seated infections of the cervix where there is a great excess of connective tissue and glands buried far beneath the surface. In these cases the entire infected tissue must either be removed or destroyed. Formerly a high amputation was done, but in our hands we failed to cure a certain percentage of cases where the leucorrheal discharge was the important factor because it was sometimes difficult to excise completely the infected mucous membrane lining the cervical canal. We now use the cautery or excise the entire diseased area with the endotherm knife. The latter is ideal sometimes when there is extensive and deep-seated infection with hypertrophy. This method requires some form of anesthesia as it is impossible to accomplish this result in the office with a light cautery. We have treated 2985 chronic cases by this method during the last ten years and seldom fail to cure the leucorrhea. During this time we have never found a case of carcinoma develop in the cervix of patients so treated. This number is too small, of course, for one to draw any conclusions as to the prophylactic results in so far as malignant change is concerned. Is it not worth while, however, for us to consider this phase of the subject? With the rapidly increasing numbers of women who are thus treated it is quite possible that in another twenty years some conclusion can be made. It is entirely speculative as to how much we may really learn about the treatment of cancer during that period. It would seem much more important for us to study the results in a large series

of cases so treated in reference to the development of cancer than to waste further time in arguments as to the best method of treatment after it has become a certainty. The more acute cases of erosion of the cervix, or cervicitis, such as follow neisserian infection or delivery, may be treated in the office with a small cautery with good results. In fact, it is the ideal method in the subacute stage of these lesions and may be employed without any special skill. Its employment saves time and is much better than the use of local applications, such as carbolic acid, nitrate of silver, etc., in the recent and milder forms, but in chronic cervicitis it will often fail to cure. We have observed cases of the chronic type so treated which were not cured of the discharge because the treatment had not removed all areas of infection. In our experience, 85 per cent of women bearing children have cervicitis of varying degree and it is seldom, even months after delivery, that we find a healthy cervix free from all evidence of inflammation. The establishment of the normal cervix after delivery is a responsibility of every one practicing obstetrics today. If this is done both puerperal sepsis and cancer may be prevented and in addition the woman may have comfort. Leucorrhea is such a common symptom among women that it is not taken as seriously by the physician as it should be and the poor woman, with the patience of her sex, toils on without complaint.

The League of Nations has proposed international war against rats for their complete extermination. It has been said that such a war, made to include flies and mosquitoes, would be the best war in history. No rats, no bubonic plague; no mosquitoes, no yellow fever or malaria; no tsetse flies, no sleeping sickness.

The world is apparently awakening to the remedy for these various ills, and, while it may be many years before we know the exact relationship between the various hosts and poisons which they communicate to man, no time will be lost in the attempt to rid ourselves of these enemies which serve as hosts to agents which lead to our destruction.

This analogy may be applied to the diseased cervix. It is our duty to awaken from a state of lethargy and teach both the profession and the public that every diseased cervix should be cured as it carries with it the possibility of malignancy. When this is actively done, cancer of the cervix, like tuberculosis, may begin to lessen in frequency. If we sit quietly by, waiting for the discovery of the actual cause and its attending phenomena, hoodwinked to the already existing facts, thousands of lives will continue to be lost, for, many years may elapse before the problem of cancer is clearly understood. In the meantime, we should not be blind to certain self-evident facts which are important elements in the prevention of cancer, even after its active cause may have been discovered.

A STUDY OF 165 CONSECUTIVE CESAREAN SECTIONS INCLUDING A COMPARISON BETWEEN 104 CLASSICAL OPERATIONS AND 61 LAPAROTRACHELOTOMIES*

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THIS comparatively small series represents the experience of one obstetrician over a period of time sufficiently long to reflect improvements in technic and modified indications, and for these reasons it seems that a review might not only be of interest but also of value.

The cases here reported were not selected but are the sum total of my series actually operated by myself during the past fifteen years, including private and consultation patients and those treated in a public ward service.

Elective operations done before onset of labor	74
Test labor varying from 5 to 96 hours	81
Patients in labor but who did not have a test	10

There were 128 private patients of whom 21 were consultation cases seen only after they had gone into labor. Ward patients numbered 37, many of whom were sent into the hospital after a long labor outside having had vaginal examinations and in some of whom the membranes had ruptured.

Many would not be considered good operative risks; for instance, one patient had been bagged, two with placenta previa had been packed outside the hospital, 50 had had from one to five vaginal examinations made, and the membranes had ruptured in 29, the time elapsing from rupture to operation varying from one to sixty hours.

One hundred twenty-three patients were operated upon at one hospital (The Rochester General) and 41 in the other four hospitals of the city. Fifteen women were operated upon twice and on five of them three sections were done from which it will be deduced that there were 135 different patients.

The distribution as to the parity of the patients is:

Para i	84	Para iv	7	Para vii	2
" ii	46	" v	1	" ix	1
" iii	20	" vi	4		

Indications.—The question of the justification for the performance of delivery by abdominal section is more unsettled perhaps than any angle from which the subject is discussed. The operation is over-

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popularized by the laity in many communities and one is as apt to be criticized by the unthinking for not having performed a cesarean section as one is for having done one. The indications in this series were many, perhaps too many, yet when one considers that of the 165 sections, 81 had had a test of labor and that of the balance, 27 were done on cases operated before, it would seem that at least one could not say that these operations were hastily done without a thorough evaluation of the conditions that were met. Another point to be considered is that in many cases more than one factor entered into the decision to operate. For instance, in seventeen cases of borderline pelvic contraction, the patient had lost one or two children from difficult deliveries previously, and I think few obstetricians, after a test of labor would be willing to attempt a high forceps extraction or delivery by version in a case with such a history.

Elderly primiparity was given as a sole indication in three cases, nevertheless all three had been subjected to trial labor, the competing procedures were high forceps, version and cesarean section. In nine other patients elderly primiparity was a secondary consideration in making a decision.

Disproportion is given as a reason for six operations, all these patients had good trial labors of from ten to twenty-one hours and the babies weighed from eight to eleven pounds.

Fibroids complicating labor in seven cases caused me to decide for abdominal delivery. In three the growth was frankly obstructive,

TABLE I. INDICATIONS

	CLASSICAL	LOW-CERVICAL	TOTAL
Flat pelvis	34	29	63
Justo minor pelvis	27	9	36
Funnel pelvis	4	1	5
Chondrodystrophic dwarf	2	0	2
Kyphoscoliosis	0	1	1
False promontory	1	0	1
Ankylosed hip	2	0	2
Disproportion	1	5	6
Mentoposterior, after test of labor	0	1	1
Previous cesarean section	8	1	9
Fibromyomas of uterus	2	5	7
Cervical cicatrix after amputation, test of labor	1	1	2
Rigidity of cervix	0	3	3
Postmaturity, elderly primip., test of labor	1	0	1
Placenta previa	5	0	5
Abruptio placentae	5	0	5
Elderly primiparity, primary sole indication	2	1	3
Eclampsia	1	0	1
Toxemia 1. Primipara of 43		1	
2. Cardionephritic primipara of 38	1		
3. Plus pulmonary tuberculosis	1		3
Cardiac disease 1. Four months, sterilized			
2. Plus large cystic goiter	2	0	2
Bicornate uterus	1	0	1
Contraction ring dystocia threatening rupture	2	3	5
Fetal asphyxia elderly primip., postmature, test	1	0	1
	104	61	165

another was in an elderly primipara becoming exhausted from a long labor, in three I believe that small multiple fibroids in the lower uterine segment so affected the musculature that dilatation, contraction, and retraction were impossible. In two of these the uterus went into tetanic contraction after a test of labor with the cervix insufficiently dilated to permit delivery below.

Previous cesarean section. In these patients there was reason to question the integrity of the uterine scar.

Technic.—Classical section was performed 104 times and laparotrachelotomy or low cervical section was performed 61 times. The first fifty-seven were of the classical type while of the last 108 sixty-one were laparotrachelotomies and forty-seven classical.

By classical cesarean section is meant an incision through the upper portion of the body of the uterus through an abdominal incision above the umbilicus, the uterus is closed in three layers, one of which is of interrupted chromic sutures. By laparotrachelotomy or low cervical section is meant the Beck two-flap modification of the original Sellheim operation later described by Kroenig.

The first laparotrachelotomy was done by me over seven years ago on a patient with a flat pelvis, seen in consultation after fifty-two hours of labor conducted with five vaginal examinations. She was becoming exhausted and delivery was imperative, she was obviously not a candidate for the usual or classical cesarean section. Although the puerperium was febrile the successful outcome of this case made such an impression on me that I have employed this technic since in any case subjected to trial labor, and more recently it has been given wider application and unless otherwise contraindicated is the method of choice for all abdominal hysterotomies. The reasons for this decision have been:

1. Sutures placed in the lower uterine segment are not subjected to as much stress from contraction and relaxation of the uterine musculature making for a stronger scar. Four patients in this series have been operated upon twice and one thrice by the low cervical technic, in all of these the scar in the uterus could not be identified.

2. A lessened liability to uterine rupture in subsequent pregnancies and labors. There have been only ten ruptures in the 3600 reported operations, 0.28 per cent as against 2.5 to 4 per cent for the classical operation.

3. Because of this the dictum "Once a cesarean always a cesarean" is not as valid today as it was a few years ago. It is safer in other words, to permit of a trial labor in cases where the indication for the original low cervical section was extrapelvic than were the original operation the classical.

4. The cervix is more tolerant of infection.

5. The lower abdomen stands infection better than the upper.

6. In case infection does occur outside the uterus it is in a location most favorable for its localization and evacuation.

7. There is much less chance for peritonitis postoperative, the most frequent cause of death following classical cesarean section.

8. With this type of operation in reserve a real test of labor may be employed in borderline pelvic contraction and it will be found that a large percentage can be delivered per vaginam.

9. It can be used in referred cases seen late in labor, unless they have been grossly mismanaged.

10. The mortality is lower, a series of 620 operations with only 6 deaths (3 of which were nonoperative deaths) in one clinic, a percentage of less than 1 as against 4 to 5 per cent in unselected series of classical sections.

11. The comfort of the patient in comparative freedom from vomiting, distension and pain, these patients present as little evidence of shock or exhaustion as one following a clean appendectomy and much less than the case subjected to a difficult instrumental delivery through the pelvis.

Details of technic in the 61 cases of laparotrachelotomy which might be briefly mentioned are:

The anesthetic preferably local plus nitrous-oxid-oxygen. No morphine given until after the delivery of the baby. The head was shelled out manually, forceps were applied only three times.

The placenta was in all cases delivered through the abdominal incision, I have never been convinced of any advantage in pushing the placenta through the cervix or in leaving it to be expelled by uterine contraction. No traction on the cord was employed in delivering the placenta, recently two cases have been reported of inversion of the uterus through the wound, ascribed to removal of the placenta by pulling upon the cord.

Suturing of the uterus is begun at the lower angle as the bleeding is more brisk than above, two rows of chromic suture, one of which is always interrupted are used in closing the uterine muscle.

The transverse uterine incision has not been employed because of greater hemorrhage at the angles of the incision, a location much more vascular than that of the vertical incision. Three conditions in which I believe the classical section is preferable to laparotrachelotomy are: (1) abruptio placentae, (2) placenta previa, (3) in very obese subjects.

Morbidity.—Although the mortality in this series is very low the amount of postoperative disturbance was sufficiently high to give me a real appreciation of the seriousness of the operation. This was due almost entirely to the type of cases encountered. Ten of the patients pursued a rather stormy convalescence; uterine infection, fat embolus and a temporary hemiplegia, postoperative tetanus and an acute cholecystitis were some of the specters which did not add to the

TABLE II

			FEVER*
Classical			
Test of labor		35	10
Shortest	5 hours		
Longest	48 "		
Average	17.3 "		
Elective		63	17
In labor		6	2
		104	29
Low Cervical			
Test of labor		46	19
Shortest	5 hours		
Longest	96 "		
Average	21.1 "		
Elective		11	4
In labor average 7 hours		4	0
		61	23
Entire Series			
Test of labor		81	29
Elective		74	21
In labor		10	2
		165	52

safety of the patients or to the peace of mind of the operator, with one exception, the first laparotrachelotomy, these were cases operated upon by the older technic.

Fifty-two were febrile, using an index of 100.4° on two consecutive days. Although abdominal wound infection was encountered there were no ventral hernias resulting. Pelvic infection was limited to the uterus. Acute gastric dilatation complicated five cases but responded to lavage and absolute rest to the stomach.

In one case known to me (No. 40 and repeat No. 54) at a subsequent labor when an attempt was made in another hospital to effect delivery through the pelvis a uterine rupture resulted. Four cases are known to have been delivered below in subsequent labors.

Mortality.—

TABLE III

	MATERNAL	FETAL
104 Classical sections	2 or 1.92%	7 or 6.5%
61 Laparotrachelotomies	0	0
165 Total operations	2 or 1.22%	7 or 4.2%

Of the last 129 sections the maternal mortality is nil.

Fetal mortality theoretically should be nil in cesarean section but in this series seven (or 4.3 per cent) babies were stillborn or died soon after birth. The first, the child of an eclamptic mother died probably during the operation as the fetal heart was strong before she went to the operating room. The remaining were all premature and five of the six were cases of abruptio placentae, the one condition

*100.4° F. on two successive days.

where it is justifiable to do a cesarean section when there is a question as to the survival of the infant, three of these mothers were toxic.

Maternal mortality was two or 1.22 per cent, these were cases Nos. 19 and 36. Number 19, eclampsia in mother, an elderly primipara who had been out to a dinner party at seven had two convulsions before my arrival as consultant at eleven. She was hospitalized and given morphine to the degree of lowering respiration markedly, her convulsions continued and at the urgent insistence of her family a section was done in the early morning hours. She continued to have convulsions and died a few hours postoperative, convulsive toxemia was the cause of death in this case. This was over eleven years ago and I wish to state it as my belief that abdominal delivery is not the treatment for eclampsia. Two surveys of cesarean sections done in two cities, viz.: New Orleans and Detroit showed a maternal mortality for cesarean section on eclamptics of 42 and 40 per cent respectively. Number 36 a primipara of thirty-six with a justo-minor pelvis was operated upon after fourteen hours of hard labor, she had a postpartum hemorrhage immediately postoperative, and in spite of various agents given to contract the uterus it never responded and before the patient could be transfused she had died.

In closing I wish to quote a paragraph from a paper I wrote four years ago reporting the first fifteen low cervical sections. "It is not claimed that by the employment of this technic all infection is obviated, it will not prevent intrauterine infection, bacteremia, extension through lymphatic channels or embolic processes, but it does in the vast majority of cases prevent the development of general peritonitis, which is by far the most frequent cause of death following cesarean section done by the old or classical method."

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(Discussion to be published in a later issue)